

AGENUS INC  
Form 10-K  
March 18, 2019

UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

Form 10-K

ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934  
For the fiscal year ended December 31, 2018

or

TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF  
1934

For the transition period from            to

Commission File Number: 000-29089

Agenus Inc.

(exact name of registrant as specified in its charter)

Delaware	06-1562417
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification No.)

3 Forbes Road, Lexington, Massachusetts 02421

(Address of principal executive offices, including zip code)

Registrant's telephone number, including area code:

(781) 674-4400

Securities registered pursuant to Section 12(b) of the Act:

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Common Stock, \$.01 Par Value    The NASDAQ Capital Market  
(Title of each class)                      (Name of each exchange on which registered)

Securities registered pursuant to Section 12(g) of the Act:

None

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act.    Yes        No

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act.    Yes        No

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days.    Yes        No

Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit such files).    Yes        No

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K (§229.405 of this chapter) is not contained herein, and will not be contained, to the best of registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K.

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a smaller reporting company, or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer                      Accelerated filer  
Non-accelerated filer                      Smaller reporting company  
Emerging growth company

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act.

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act).    Yes        No

The aggregate market value of voting stock held by non-affiliates of the registrant as of June 29, 2018 (the last trading day of the registrant's second fiscal quarter of 2018) was: \$194.0 million. There were 134,205,374 shares of the registrant's Common Stock outstanding as of March 11, 2019.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the Registrant's Definitive Proxy Statement relating to the 2019 Annual Meeting of Stockholders, which the registrant intends to file with the Securities and Exchange Commission pursuant to Regulation 14A within 120 days after the end of the registrant's fiscal year ended December 31, 2018, are incorporated by reference into Part III of this Report.

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Note Regarding Forward-Looking Statements

This Annual Report on Form 10-K and other written and oral statements the Company makes from time to time contain forward-looking statements. You can identify these forward-looking statements by the fact they use words such as “could,” “expect,” “anticipate,” “estimate,” “target,” “may,” “project,” “guidance,” “intend,” “plan,” “believe,” “will,” “opportunity,” “future” and other words and terms of similar meaning. Forward-looking statements include discussion of future operating or financial performance. You also can identify forward-looking statements by the fact that they do not relate strictly to historical or current facts. Forward-looking statements involve risks and uncertainties that could delay, divert or change any of them, and could cause actual outcomes to differ materially. These statements relate to, among other things, our business strategy, our research and development, our product development efforts, our ability to commercialize our product candidates, the activities of our licensees, our prospects for initiating partnerships or collaborations, the timing of the introduction of products, the effect of new accounting pronouncements, our future operating results and our potential profitability, availability of additional capital as well as our plans, objectives, expectations, and intentions.

Although we believe we have been prudent in our plans and assumptions, no assurance can be given that any goal or plan set forth in forward-looking statements can be achieved, and readers are cautioned not to place undue reliance on such statements, which speak only as of the date of this report. We undertake no obligation to release publicly any revisions to forward-looking statements as a result of new information, future events or otherwise.

The risks identified in this Annual Report on Form 10-K, including, without limitation, the risks set forth in Part I-Item 1A. “Risk Factors,” could cause actual results to differ materially from forward-looking statements contained in this Annual Report on Form 10-K. We encourage you to read those descriptions carefully. Such statements should be evaluated in light of all the information contained in this document.

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## PART I

### Item 1. Business

#### Our Business

We are a clinical-stage immuno-oncology (“I-O”) company with a pipeline of immune modulating antibodies, cancer vaccines, adjuvants and adoptive cell therapies - dedicated to becoming a leader in the discovery and development of innovative combination therapies and committed to bringing effective medicines to patients with cancer. Our business is designed to drive success in I-O through speed, innovation and effective combination therapies. We believe that combination therapies and a deep understanding of each patient’s cancer will drive substantial expansion of the patient population benefiting from current I-O therapies. In addition to a diverse pipeline, we have assembled fully integrated end-to-end capabilities including novel target discovery, antibody generation, cell line development and good manufacturing practice (“GMP”) manufacturing. We believe that these fully integrated capabilities enable us to produce novel candidates on timelines that are shorter than the industry standard. Leveraging from our science and capabilities, we have forged important partnerships to advance our innovation.

We believe the next generation of cancer treatment will build on clinically validated antibodies targeting CTLA-4 and PD-1 combined with novel immunomodulatory agents designed to address underlying tumor immune-escape mechanisms.

Our immunotherapy pipeline features vaccines, adjuvants, immunomodulatory and tumor microenvironment modifying antibodies, including our proprietary lead antibodies, AGEN1884 (an anti-CTLA-4 of the same IgG1 subclass as Yervoy®), and AGEN2034 (an anti-PD-1 antibody). These proprietary antibodies bind to validated targets—CTLA-4 and PD-1—and are our most advanced clinical stage combination agents with registrational potential in cervical cancer. We are aiming to develop, register and launch these products with a first potential biologics license application (“BLA”) filing as early as 2020 for both AGEN2034 monotherapy and combination therapy with AGEN1884 in second line cervical cancer. The overall strength of our pipeline, which includes potential first-in-class and best-in-class assets, is expected to drive our ability to meet individual patients’ needs.

In addition to our lead programs, Agenus scientists have leveraged our internal discovery and translational platforms and powerful algorithms to develop a pipeline of molecules that are intended to address key aspects of antitumor immunity and tumor resistance mechanism. For tumors not yet visible to the immune system, we are leveraging our immune educating neoantigen vaccine platform, designed to target mutationally based and biochemically based (phosphorylated) neoantigens (AutoSynVax and PhosphoSynVax) to prime the immune system to attack tumors. These vaccines may be applicable for patients where checkpoint modulating (“CPM”) antibodies alone are not sufficient to bring about tumor control. To further improve patient response rates, Agenus scientists are developing therapies intended to address mechanisms of immune evasion and therapeutic resistance. These include “multi-specific” antibodies that are designed to condition the tumor microenvironment and augment the activity of immune cells. We and our partners are on track to begin clinical trials with these assets in 2019. With this diverse pipeline, we are positioned to potentially deliver combination therapies with the goal to enhance response rates and benefit patients who are unresponsive to current immunotherapies.

In 2017, we formed a subsidiary, AgenTus Therapeutics, to bring innovative living drugs to cancer patients. AgenTus’ pipeline includes T cell receptors (TCR) and chimeric antigen receptors (CAR) formulated in both autologous and allogeneic cell formats. We anticipate filing our first cell therapy IND through AgenTus and advancing our differentiated allogeneic cell format towards an IND in 2019.

To succeed in I-O, innovation and speed are paramount. We are a vertically integrated biotechnology company equipped with a suite of technology platforms to advance from novel target identification (Retrocyte Display, SECANT, Agenus Immunogenic Platform (“AIM”), functional genomics and ligandomics) through manufacturing for clinical trials of antibodies and vaccines.

Our common stock is currently listed on The Nasdaq Capital Market under the symbol “AGEN.”

#### Our Vision

We believe that combination therapies and a deep understanding of each patient’s cancer will be key drivers of success in substantially expanding the patient population benefiting from current I-O therapies. In addition, delivering innovation with speed is critical for our future success, as drug development timelines in oncology shorten while product obsolescence rates climb. We believe our fully integrated, end-to-end capabilities from novel target discovery, antibody generation, cell line development, to GMP manufacturing, together with a comprehensive portfolio consisting of antibody-based therapeutics, adjuvants and cancer vaccines, will uniquely position us to produce novel therapies on accelerated timelines. We believe that a balanced pipeline of product candidates should focus on both validated targets as well as novel targets designed to address tumor escape mechanisms. CTLA-4 and PD-1 antagonists are recognized as the first clinically validated immunotherapy combination. These, in combination with innovative immunomodulatory antibodies or immune education vaccines, could be a focal point of the next generation of I-O combinations. Therefore, we plan to develop, register and launch our proprietary antibodies targeting PD-1 and CTLA-4 aggressively through the clinic and expand with novel combination therapies designed to improve clinical response and the durability of response of existing therapies.



## Our Strategy

Our strategy is to bring innovative combination therapies for cancer patients to substantially expand the patient population benefiting from current I-O therapies. Our diverse pipeline of antibodies, vaccines and adjuvants enable us to pursue optimal combinations for optimal efficacy. We are pursuing a tiered risk profile and targeting compressed timelines for regulatory filings. In 2018, we met with the FDA and expect that each of our lead anti-CTLA-4 (AGEN1884) and anti-PD-1 (AGEN2034) trials are designed to support a BLA filing in second-line cervical cancer as early as 2020. We believe that we are positioned to take advantage of accelerated pathways for approval with a relatively small number of patients and surrogate or short-term endpoints in our trials. In addition, we plan to pursue select indications to further expedite market entry.

Our strategy for our more novel, earlier stage programs include (i) pursuit of effective I-O antibody, vaccine and cell-therapy combinations with CTLA-4 and/or PD-1 targeted antibodies as the backbone and (ii) advancement of our differentiated antibody programs such as our bispecific programs, a next generation anti-CTLA-4, and differentiated CD137 and TIGIT antibodies.

Part of our strategy is to develop and commercialize some of our product candidates by continuing our existing arrangements with collaborators and licensees and by entering into new collaborations. We are also pursuing novel financial mechanisms to support programs such as AGEN2034, including our recently announced launch of Biotech Electronic Security Tokens (BEST). See “Risk Factors—Risks Relating to Our Tokens.”

## Our Assets

Our I-O assets include antibody-based therapeutics, cancer vaccine platforms and adjuvants. Our proprietary CTLA-4 and PD-1 antagonists are in clinical development; we are one of only a few companies to have proprietary anti-CTLA-4 and anti-PD-1 antibodies in clinical combinations.

To complement our portfolio of foundational CPMs, we and our partners have pre-clinical antibodies targeting tumor escape mechanisms and therapeutic resistance. These include potential best-in-class and first-in-class assets such as our next-generation anti-CTLA-4 (AGEN1181) and TIGIT (AGEN1307), as well as CD137 (AGEN2373) and bispecific antibodies that are partnered with Gilead.

Further, our neoantigen vaccine platforms include: (i) Individualized AutoSynVax™ (ASV™), which targets the unique antigens expressed by a patient’s own tumor, and (ii) off-the-shelf (or pre-manufactured) PhosphoSynVax™ (PSV™), which targets antigens expressed across patients and tumors, thereby seeking to treat broader categories of patients. Our vaccines are powered by our proprietary adjuvant, QS-21 Stimulon®. We plan to evaluate ASV in combination with checkpoint antibodies in 2019 and we are advancing preclinical development of PSV.

Our proprietary QS-21 Stimulon® is believed to be one of the most potent adjuvants known. QS-21 Stimulon® is a key component in several GSK vaccines, including GSK’s Shingrix, which has demonstrated greater than 90% efficacy, as well as the first ever malaria vaccine, Mosquirix®. Shingrix sales are substantially ahead of forecasts, making additional milestones from our royalty transaction with HCR much more likely. QS-21 is being used in numerous other clinical-stage vaccines, including our own cancer vaccines. Recently, the Bill & Melinda Gates Foundation awarded us a grant to develop an alternative, plant cell culture-based manufacturing process to ensure the continuous future supply of QS-21 Stimulon® adjuvant.

## Our Antibody Discovery Platforms and CPM Programs

Checkpoint antibodies regulate immune response against pathogens that invade the body and are achieving positive outcomes in a number of cancers that were untreatable only a few years ago. Two classes of checkpoint targets include:

1. inhibitory checkpoints that help suppress an immune response in order to prevent excessive immune reaction resulting in undesired inflammation and/or auto-immunity, and
2. stimulatory checkpoints that can enhance or amplify an antigen-specific immune response.

We possess a suite of antibody discovery platforms that are designed to drive the discovery of future CPM antibody candidates. We are planning to employ a variety of techniques to identify and optimize mono-specific and multi-specific antibody candidates, internally.

Our anti-CTLA-4 and anti-PD-1 programs (AGEN1884 and AGEN2034, respectively) are in clinical trials that included a Phase 1 dose escalation with expansion cohorts in multiple solid tumors. These molecules are now in expansion trials with both anti-PD-1 monotherapy and anti-PD-1 and anti-CTLA-4 combination trials for patients with second-line cervical cancer that are designed to support one or more BLA filings as soon as 2020. In 2018, we presented data on our AGEN1884 and AGEN2034 programs at major oncology conferences, including the American Society of Clinical Oncology (“ASCO”) conference in June 2018 and the European Society for Medical Oncology (ESMO) congress in October 2018. In addition, we presented pre-clinical data on our Gilead-partnered anti-CD137 (AGEN2373), and our Incyte-partnered programs anti-TIM-3 and anti-LAG-3 antibodies at the American Association for Cancer Research (“AACR”) conference in April 2018 and the Society for Immunotherapy of Cancer (“SITC”) conference in November 2018. Our early clinical data demonstrated a clinical benefit (i.e., complete response, partial response or disease

stabilization) in more than 60% of patients treated with AGEN1884 and AGEN2034.

As of our latest data update in the fourth quarter of 2018, we have reported the following:

• We treated more than 140 patients with AGEN1884 and/or AGEN2034 and observed clinical benefit in more than 60% of them

• In our AGEN2034 (anti-PD-1) monotherapy trial, 68% of evaluable patients with metastatic and/or locally advanced solid tumors experienced clinical benefit. We presented data showing that:

o Among 38 subjects from Phase 1 of the study, three patients displayed partial response to therapy (i.e., tumors shrunk) and 23 patients displayed stable disease (i.e., tumor size was unchanged) during the follow-up period (median of 191 days or 27 weeks).

o In the ongoing Phase 2 expansion portion of this study (NCT03104699) in advanced refractory cervical cancer, three out of seven (43%) of evaluable patients experienced a clinical benefit as of July 2018. Data continues to accumulate.

o AGEN2034 appeared to be clinically active and well-tolerated.

• In our AGEN2034 (anti-PD-1) plus AGEN1884 (anti-CTLA-4) combination trial, 63% of patients with ovarian, breast, and soft tissue sarcomas showed clinical benefit, including an objective durable response in a patient with ovarian cancer.

With respect to our novel discovery pipeline, our most advanced asset is our next generation anti-CTLA-4 antibody, an IgG1 anti-CTLA-4 antagonist. Based on preclinical data, we believe that this molecule has potential advantages over competing anti-CTLA-4 molecules, including:

- (1) potential to induce enhanced T cell priming via the engineered Fc region, as T cell priming is a crucial step in generating potent immune responses against cancer,
- (2) increased potential to deplete intratumoral regulatory T cells, which represent a significant barrier to successful anti-cancer immune responses,
- (3) better combination potential with other antitumor or immunomodulatory antibodies, vaccines, and targeted therapies and
- (4) potential therapeutic benefit to a wider patient population, including the estimated 40% of patients who are unlikely to fully benefit from the first generation CTLA-4 therapies due to a genetic predisposition.

We filed an IND for AGEN1181 in the fourth quarter of 2018 and expect to initiate clinical trials in 2019.

#### Partnered CPM Programs

In December 2018, we entered into a series of agreements with Gilead Sciences, Inc. (“Gilead”) to collaborate on the development and commercialization of up to five novel I-O therapies. Pursuant to the collaboration agreements, we received an upfront cash payment from Gilead of \$120.0 million following the closing in January 2019 and are eligible to receive up to an additional \$1.7 billion in aggregate potential fees and milestones. At closing, Gilead received worldwide exclusive rights to our bispecific antibody, AGEN1423. Gilead also received the exclusive option to license exclusively AGEN1223, a bispecific antibody, and AGEN2373, a monospecific antibody. We recently filed INDs for AGEN1423 and AGEN1223 and are planning to file an IND for AGEN2373 in the first half of 2019. We are responsible for developing the option programs up to the option decision points, at which time Gilead may acquire exclusive rights to the programs on option exercise. For either, but not both, of the option programs, we have the right to opt-in to share Gilead’s development and commercialization costs in the United States in exchange for a profit (loss) share on a 50:50 basis and revised milestone payments. Gilead also received the right of first negotiation for two additional, undisclosed preclinical programs. At the closing, Gilead also purchased 11,111,111 shares of Agenus common stock for \$30.0 million pursuant to a stock purchase agreement.

In January 2015, we entered into a collaboration with Incyte Corporation (“Incyte”) to discover, develop and commercialize novel immuno-therapeutics using our antibody platforms. The collaboration was initially focused on four CPM programs targeting GITR, OX40, TIM-3 and LAG-3, and in November 2015, we expanded the alliance by adding three novel undisclosed CPM targets. Pursuant to the terms of the original agreement, Incyte paid us \$25.0 million in upfront cash. Targets under the collaboration were designated as either profit-share programs, where the parties shared all costs and profits equally, or royalty-bearing programs, where Incyte funded all costs, and we were eligible to receive milestones and royalties. Under the original collaboration agreement, programs targeting GITR, OX40 and two of the undisclosed targets were designated as profit-share programs, while the other targets were royalty-bearing programs. For each profit-share product, we were eligible to receive up to \$20.0 million in future contingent development milestones. For each royalty-bearing product, we were eligible to receive (i) up to \$155.0 million in future contingent development, regulatory, and commercialization milestones and (ii) tiered royalties on global net sales at rates generally ranging from 6%-12%. Concurrent with the execution of the original collaboration agreement, we and Incyte also entered into a stock purchase agreement pursuant to which Incyte purchased approximately 7.76 million shares of our common stock for an aggregate purchase price of \$35.0 million. In February 2017, we and Incyte amended the terms of the original collaboration agreement to, among other things, convert the GITR and OX40 programs from profit-share to royalty-bearing programs with royalties on global net sales at a flat

15% rate for each. In addition, the profit-share programs relating to two undisclosed targets were removed from the collaboration, with one reverting to Incyte and one to Agenus (the latter being our TIGIT antibody program), each with royalties on global net sales at a flat 15% rate. The remaining three royalty-bearing programs in the collaboration targeting TIM-3, LAG-3 and one undisclosed target remain unchanged, and there are no more profit-share programs under the collaboration. Pursuant to the amended agreement, we received accelerated milestone payments of \$20.0 million from Incyte related to the clinical development of INCAGN1876 (anti-GITR agonist) and INCAGN1949 (anti-OX40 agonist). Concurrent with the execution of the amendment agreement, we and Incyte entered into a separate stock purchase agreement whereby Incyte purchased an additional 10 million shares of our common stock for an aggregate purchase price of \$60.0 million. Incyte advanced both INCAGN1876 (anti-GITR agonist) and INCAGN1949 (anti-OX40 agonist) into the clinic in 2016. INCAGN1876 is currently in a Phase 1/2 trial exploring its safety, tolerability, and efficacy in combination with immune therapies, ipilimumab and nivolumab, in advanced or metastatic malignancies such as advanced or metastatic endometrial cancer, gastric cancer (including stomach, esophageal, and gastroesophageal junction), and squamous cell carcinoma of the head and neck. INCAGN1949 is currently in a Phase 1/2 trial exploring its safety, tolerability, and efficacy in combination with immune therapies, ipilimumab and nivolumab, in advanced or metastatic malignancies such as advanced or metastatic urothelial carcinoma or RCC. In 2018, Incyte initiated clinical trials for their INCAGN2385 (LAG-3) and INCAGN2390 (TIM-3) programs.

In April 2014, we entered into a collaboration and license agreement with Merck to discover and optimize fully-human antibodies against two undisclosed CPM targets. In 2016, Merck selected a lead product candidate against one of the undisclosed targets to advance into preclinical studies, and subsequently initiated a Phase 1 clinical trial with the undisclosed antibody in August 2018. Under the terms of the agreement, Merck is responsible for all future product development expenses for the selected antibody candidate, and Agenus is eligible to receive up to \$95.0 million in potential milestones plus royalties on any future sales.

On September 20, 2018, we, through our wholly-owned subsidiary, Agenus Royalty Fund, LLC, entered into a Royalty Purchase Agreement (the "XOMA Royalty Purchase Agreement") with XOMA (US) LLC ("XOMA US"). Pursuant to the terms of the XOMA Royalty Purchase Agreement, XOMA US paid us \$15.0 million at closing in exchange for the right to receive 33% of the future royalties and 10% of the future milestones that we are entitled to receive from Incyte and Merck, net of certain of our obligations to a third party and excluding the milestone we received from Incyte in the fourth quarter of 2018. After taking into account our obligations under the XOMA Royalty Purchase Agreement, as of December 31, 2018, we remain eligible to receive up to \$450.0 million and \$85.5 million in potential development, regulatory and commercial milestones from Incyte and Merck, respectively.

We also have a collaboration agreement with Recepta Biopharma SA for the development of our antibodies targeting CTLA-4 and PD-1, which gives Recepta certain rights to South American countries. We expect to continue exploring additional future collaborations.

#### Vaccine Platforms

Our current vaccine platforms for the treatment of cancer, and potentially other indications, include our HSP based Prophage vaccine candidates, and our fully synthetic, neoantigen vaccine candidates, ASV and PSV.

HSPs are a group of proteins present at high levels in most mammalian cells. Their expression is increased when cells are exposed to elevated temperatures or other stresses. A potential role for HSPs in regulating immune responses was revealed when it was first discovered that HSP complexes purified from cancer cells produced immunity to cancer, whereas HSP complexes purified from normal tissue did not. This discovery led to the understanding that HSPs bind to and carry a broad sampling of the protein environment within cells, including mutant proteins that might arise from genetic mutations within cancer cells. It was further shown that immunization with HSP complexes purified from tumors generate both CD4 and CD8 positive T-cell immune responses. These activated T-cells target the cancer cells of the tumor, from which the HSP complexes were derived, for destruction. Thus, HSP complexes isolated from

cancer cells may be particularly helpful in mediating successful immunization. Since HSPs are expressed in all tumor cells, the approach of immunizing with the HSP complexes isolated from a particular tumor may be broadly applicable to a variety of cancer types. We believe that we pioneered the use of gp96, an HSP, purified from a patient's own tumor tissue, as a way to make I-O vaccine candidates.

#### Prophage Vaccine Candidates

Our early vaccine technology, Prophage (HSPPC-96), is an autologous cancer vaccine therapy derived from cancer tissues that are surgically removed from an individual patient designed to contain a broad sampling of potentially antigenic mutant proteins to educate the patient's immune system to seek out and destroy cancer. To date, more than 1,000 patients have been treated with Prophage. Data reported at ASCO in 2015 demonstrated that patients with newly diagnosed GBM (ndGBM) with lower immune suppression (measured by peripheral PD-L1 expression) had an improved response to vaccine. To further explore these findings, we announced a Phase 2 clinical trial collaboration with the National Cancer Institute ("NCI") to evaluate Prophage in combination with pembrolizumab (Keytruda®). The trial is being conducted by the Brain Tumor Trials Collaborative ("BTTC"), led by Dr. Mark Gilbert, Chief of the Neuro-Oncology Branch at the NCI Center for Cancer Research with product provided by Agenus and Merck. The trial is ongoing.

## Neoantigen Vaccine Platforms

Our neoantigen vaccine platforms include: (i) individualized AutoSynVax™ (ASV™), which targets the unique antigens expressed by a patient's own tumor, and (ii) off-the-shelf (or pre-manufactured) PhosphoSynVax™ (PSV™), which targets antigens expressed across patients and tumors, potentially enabling us to treat broader categories of patients.

Our neoantigen vaccines are designed with unique features, intending to confer important advantages: (1) proprietary methods to develop an effective and relevant "Blueprint" of immunogenic neoantigens for each patient; (2) HSPs to efficiently deliver neoantigens to the right immune cells to activate an anti-cancer immune response. Our proprietary linker technology is designed to enable efficient neoantigen loading for a robust cancer specific immune response with significantly less peptide; and (3) QS-21 Stimulon® adjuvant, a potent immune stimulator now in GSK's commercial shingles vaccine, Shingrix.

Mutation-based neo-epitopes, which will form the basis for the immunogens used in ASV, appear to be almost always particular to a given patient. Therefore, ASV is a largely individualized vaccine product candidate. With a small amount of a patient's tumor as a sample, our ASV program is designed to utilize next generation sequencing technologies coupled with complex bioinformatics algorithms to identify mutations in a tumor's DNA and RNA. Once these mutations have been identified, we plan to manufacture synthetic peptides encoding these neoepitopes, load these peptides on to our recombinant HSP70 and deliver a fully synthetic polyvalent vaccine to the patient. This program is based on the hypothesis that the HSP70 platform would shuttle the mutated peptides to sites where they could be recognized by the immune system and elicit a cytotoxic and helper T cell response in patients with cancer.

Biochemically based neoantigens, such as those arising from dysregulated phosphorylation of various proteins in malignant cells, can serve as a tumor fingerprint across a broad histology of tumors. Through our acquisition of PhosImmune, we have a portfolio of proprietary phosphorylated antigenic targets that can be used for therapeutic development. PSV is a vaccine candidate designed to induce immunity against this novel class of tumor specific neoepitopes known as Phosphopeptides ("PTTs"). PSV is intended to induce cellular immunity to abnormal phosphopeptide neoepitopes that are characteristic of these various forms of cancer. We believe PTTs are among the most promising candidates for anti-cancer immunity, as patients with PTT immunity have been shown to have better outcomes than those without PTT immunity. We have amassed a proprietary library of more than 2,000 PTTs. Many of these PTTs are shared among many cancer patients and across multiple tumor types. We are using these PTTs for developing multiple off-the-shelf vaccines. PSV is based on our vaccine platform and includes our proprietary QS-21 Stimulon adjuvant and heat-shock protein backbone. We are developing multiple indication-specific PSV offerings, with lead programs in acute myeloid leukemia (AML) and colorectal cancer (CRC). By leveraging our proprietary vaccine platform which has already demonstrated clinical safety and immunogenicity, we intend to advance at least one PSV formulation into the clinic in 2019.

## QS-21 Stimulon Adjuvant

QS-21 Stimulon is an adjuvant, which is a substance added to a vaccine or other immunotherapy that is intended to enhance an immune response to the target antigens. QS-21 Stimulon is a natural product, a triterpene glycoside, or saponin, purified from the bark of the Chilean soapbark tree, *Quillaja saponaria*. QS-21 Stimulon has the ability to stimulate an antibody-mediated immune response and has also been shown to activate cellular immunity. It has become a key component in the development of investigational preventive vaccine formulations across a wide variety of diseases. These studies have been carried out by academic institutions and pharmaceutical companies in the United States and internationally. A number of these studies have shown QS-21 Stimulon to be significantly more effective in stimulating immune responses than aluminum hydroxide or aluminum phosphate, the adjuvants most commonly used in approved vaccines in the United States today. In January 2019, we announced that the Bill & Melinda Gates Foundation awarded us a grant to develop an alternative, plant cell culture-based manufacturing process to ensure the continuous future supply of QS-21 Stimulon adjuvant.

### Partnered QS-21 Stimulon Programs

In 2006, we entered into a license agreement and a supply agreement with GSK for the use of QS-21 Stimulon (the “GSK License Agreement” and the “GSK Supply Agreement,” respectively). In 2009, we entered into an Amended and Restated Manufacturing Technology Transfer and Supply Agreement (the “Amended GSK Supply Agreement”) under which GSK has the right to manufacture all of its requirements of commercial grade QS-21 Stimulon. GSK is obligated to supply us, or our affiliates, licensees, or customers, certain quantities of commercial grade QS-21 Stimulon for a stated period of time. In March 2012, we entered into a First Right to Negotiate and Amendment Agreement amending the GSK License Agreement and the Amended GSK Supply Agreement to clarify and include additional rights for the use of QS-21 Stimulon (the “GSK First Right to Negotiate Agreement”). In addition, we granted GSK the first right to negotiate for the purchase of Agenus or certain of our assets, which expired in March 2017. As consideration for entering into the GSK First Right to Negotiate Agreement, GSK paid us an upfront cash payment of \$9.0 million, \$2.5 million of which was creditable toward future royalty payments. We refer to the GSK License Agreement, the Amended GSK Supply Agreement and the GSK First Right to Negotiate Agreement collectively as the GSK Agreements. In 2017, we received a final milestone payment of \$1.0 million from GSK and are no longer entitled to any additional milestone payments under the GSK Agreements. Under the terms of the Agreement, we are generally entitled to receive a 2% royalty on net sales of prophylactic vaccines for a period of 10 years after the first commercial sale of a resulting GSK product, which was triggered with GSK’s first commercial sale of Shingrix in 2017. Notably, we have already monetized and sold this entire royalty stream as discussed in more detail below.



The GSK License and Amended GSK Supply Agreements may be terminated by either party upon a material breach if the breach is not cured within the time specified in the respective agreement. The termination or expiration of the GSK License Agreement does not relieve either party from any obligation which accrued prior to the termination or expiration. Among other provisions, the license rights granted to GSK survive expiration of the GSK License Agreement. The license rights and payment obligations of GSK under the Amended GSK Supply Agreement survive termination or expiration, except that GSK's license rights and future royalty obligations do not survive if we terminate due to GSK's material breach unless we elect otherwise. We do not incur clinical development costs for products partnered with GSK.

In September 2015, we monetized a portion of the royalties associated with the GSK License Agreement to an investor group led by Oberland Capital Management for up to \$115.0 million in the form of a non-dilutive royalty transaction. Under the terms of a note purchase agreement with the investor group (the "Note Purchase Agreement"), we received \$100.0 million at closing for which the investors had the right to receive 100% of our worldwide royalties under the GSK License Agreement on sales of GSK's Shingrix and malaria (RTS,S) prophylactic vaccine products that contain our QS-21 Stimulon adjuvant to pay down principle and interest. In November 2017, and pursuant to the Note Purchase Agreement, we received an additional \$15.0 million in cash from the investors based on the approval of Shingrix by the FDA. Pursuant to the terms of this transaction, we retained the right to receive all royalties from GSK after all principal, interest and other obligations were satisfied under the Note Purchase Agreement. The Note Purchase Agreement also allowed us to buy back the loan and extinguish the notes early under pre-specified terms, which we did in January 2018.

In January 2018, we sold 100% of all royalties we were entitled to receive from GSK to Healthcare Royalty Partners III, L.P. and certain of its affiliates (collectively, "HCR") and used the proceeds to extinguish the debt under the Note Purchase Agreement. HCR paid approximately \$190.0 million at closing for the royalty rights, of which approximately \$161.9 was used to extinguish the prior notes, yielding us approximately \$28.0 million in net proceeds. We are also entitled to receive up to \$40.35 million in milestone payments from HCR based on sales of GSK's vaccines as follows: (i) \$15.1 million upon reaching \$2.0 billion last-twelve-months net sales any time prior to 2024 and (ii) \$25.25 million upon reaching \$2.75 billion last-twelve-months net sales any time prior to 2026. We would owe a reverse milestone payment of approximately \$25.9 million to HCR in 2021 if neither of the following sales milestones are achieved: (i) 2019 sales of the GSK vaccines exceed \$1.0 billion or (ii) 2020 sales of the GSK vaccines exceed \$1.75 billion (the "Rebate Payment"). As part of the transaction, we provided a guaranty for the potential Rebate Payment and secured the obligation with substantially all of our assets pursuant to a security agreement, subject to certain customary exceptions and excluding all assets necessary for AgenTus Therapeutics, Inc. In February 2019, GSK reported that Shingrix sales for 2018, its first full year on the market, were over \$1.0 billion.

## Manufacturing

### Manufacturing CPM Antibodies

In December 2015, we acquired an antibody manufacturing pilot plant in Berkeley, CA from XOMA Corporation ("XOMA"), which we refer to as "Agenus West." A team of former XOMA employees with valuable chemistry, manufacturing and controls experience joined us and continue to operate the facility. In addition, in February 2017, we amended our collaboration with Incyte, transferring manufacturing responsibilities for all antibodies under the collaboration to them. This includes antibodies targeting GITR, OX40, TIM-3, LAG-3 and one undisclosed target. We have transferred the manufacturing know how to Incyte to support these endeavors and allow Agenus to focus on the manufacture of antibodies for some of our own CPM programs and those of existing and potential third-party collaborators. Since the acquisition of Agenus West, we have made significant improvements in the plant, and added additional headcount increasing both scale and capacity. Agenus West is currently producing antibody drug substance for our lead programs. We have been able to deliver clinical grade material from research cell banks in approximately four months, which we believe to be three to four times faster than the industry average. Agenus West utilizes cutting-edge technology platforms, enabling us to be self-reliant and giving us the advantage of manufacturing speed,

cost efficiency, operational flexibility and manufacturing technology transfer to commercial scale partners—all with desired product quality, with the ultimate goal of benefiting patients.

#### Manufacturing Cancer Vaccines

We manufacture our cancer vaccine candidates in our Lexington, MA facility.

Each Prophage vaccine is manufactured using a patient's own tumor. After the patient undergoes surgery to remove cancerous tumor tissue, the tumor is shipped frozen in a specially designed kit provided by us to our Lexington, Massachusetts facility. The turnaround time from the date of surgery to delivery of vaccine is approximately three to four weeks, which generally fits well with the patient's recovery time from surgery.

ASV and PSV vaccine candidates are manufactured using HSP70 loaded with synthetic peptide synthesized by approved manufacturers. The sequence of the peptides is determined by sequencing and analysis of patient and tumor DNA and RNA and run through complex algorithms by our bioinformatics group who have specialized knowledge of the attributes required to elicit immune responsiveness. This process takes several weeks, after which the manufactured vaccine undergoes extensive quality testing, including sterility testing, which takes a further two weeks.

We have established, within a single facility, well-defined, cost efficient vaccine manufacturing under GMPs, including bioanalytical, quality control and quality assurance, logistics, distribution and supply chain management. After manufacturing, Prophage and ASV vaccine candidates are tested and released by our analytical and quality systems staff. The quality control organization performs a series of release assays designed to ensure that the product meets all applicable specifications. Our quality assurance staff also reviews manufacturing and quality control records prior to batch release in an effort to assure conformance with current GMP (“cGMP”) as mandated by the FDA and foreign regulatory agencies.

Our manufacturing staff is trained and routinely evaluated for conformance to rigorous manufacturing procedures and quality standards. This oversight is intended to ensure compliance with FDA and foreign regulations and to provide consistent vaccine output. Our quality control and quality assurance staff is similarly trained and evaluated as part of our effort to ensure consistency in the testing and release of the product, as well as consistency in materials, equipment and facilities.

#### QS-21 Stimulon

Except in the case of GSK, we have retained worldwide manufacturing rights for QS-21 Stimulon, and we have the right to subcontract manufacturing for QS-21 Stimulon. In addition, under the terms of our agreement with GSK, upon request by us, GSK is committed to supply certain quantities of commercial grade QS-21 Stimulon to us and our licensees for a fixed period of time.

#### Intellectual Property Portfolio

We seek to protect our technologies through a combination of patents, trade secrets and know-how, and we currently own, co-own or have exclusive rights to approximately 25 issued United States patents and approximately 75 issued foreign patents. We also own, co-own or have exclusive rights to approximately 35 pending United States patent applications and approximately 180 pending foreign patent applications. We may not have rights in all territories where we may pursue regulatory approval for our product candidates.

Through various acquisitions, we own, co-own, or have exclusive rights to a number of patents and patent applications directed to various methods and compositions, including methods for identifying therapeutic antibodies and product candidates arising out of such entities’ technology platforms. In particular, we own patents and patent applications relating to our Retrocyte Display technology platform, a high throughput antibody expression platform for the identification of fully-human and humanized monoclonal antibodies. This patent family is projected to expire between 2029 and 2031. We own, co-own, or have exclusive rights to patents and patent applications directed to various methods and compositions, including a patent directed to methods for identifying phosphorylated proteins using mass spectrometry. This patent is projected to expire in 2023. In addition, as we advance our research and development efforts with our institutional and corporate collaborators, we are seeking patent protection for certain newly identified therapeutic antibodies and product candidates. We can provide no assurance that any of our patents, including the patents that we acquired or in-licensed, will have commercial value, or that any of our existing or future patent applications, including the patent applications that were acquired or in-licensed, will result in the issuance of valid and enforceable patents. Our issued patents covering Prophage vaccine and methods of use thereof, alone or in combination with other agents, expired or will expire at various dates between 2015 and 2024. In particular, our issued U.S. patents covering Prophage composition of matter expired in 2015. In addition, our issued patents covering QS-21 Stimulon composition of matter expired in 2008. We continue to explore means of extending the life cycle of our patent portfolio.

Various patents and patent applications have been exclusively licensed to us by the following entities:

University of Virginia

In connection with our acquisition of PhosImmune in December 2015, we obtained exclusive rights to a portfolio of patent applications and one issued patent relating to PTTs under a patent license agreement with the University of Virginia (“UVA”). The UVA license gives us exclusive rights to develop and commercialize the PTT technology. Under the license agreement, we will pay low to mid-single digit running royalties on net sales of PTT products, and a modest flat percentage of sublicensing income. In addition, we may be obligated to make milestone payments of up to \$2.7 million for each indication of a licensed PTT product to complete clinical trials and achieve certain sales thresholds. The term of the UVA license agreement ends when the last of the licensed patents expires or becomes no longer valid. The UVA license agreement may be terminated as follows: (i) by UVA in connection with our bankruptcy or cessation of business relating to the licensed technology, (ii) by UVA if we commit a material, uncured breach or (iii) by us for our convenience on 180 days written notice.

#### Ludwig Institute for Cancer Research

On December 5, 2014, our wholly-owned subsidiary, Agenus Switzerland Inc. (formerly known as 4-Antibody AG) (“4-AB”), entered into a license agreement with the Ludwig Institute for Cancer Research Ltd. (“Ludwig”), which replaced and superseded a prior agreement entered into between the parties in May 2011. Pursuant to the terms of the license agreement, Ludwig granted 4-AB an exclusive, worldwide license under certain intellectual property rights of Ludwig and Memorial Sloan Kettering Cancer Center arising from the prior agreement to further develop and commercialize GITR, OX40 and TIM-3 antibodies. On January 25, 2016, we and 4-AB entered into a second license agreement with Ludwig, on substantially similar terms, to develop CTLA-4 and PD-1

antibodies. Pursuant to the December 2014 license agreement, 4-AB made an upfront payment of \$1.0 million to Ludwig. The December 2014 license agreement also obligates 4-AB to make potential milestone payments of up to \$20.0 million for events prior to regulatory approval of licensed GITR, OX40 and TIM-3 products, and potential milestone payments in excess of \$80.0 million if such licensed products are approved in multiple jurisdictions, in more than one indication, and certain sales milestones are achieved. Under the January 2016 license agreement, we are obligated to make potential milestone payments of up to \$12.0 million for events prior to regulatory approval of CTLA-4 and PD-1 licensed products, and potential milestone payments of up to \$32.0 million if certain sales milestones are achieved. Under each of these license agreements, we and/or 4-AB will also be obligated to pay low to mid-single digit royalties on all net sales of licensed products during the royalty period, and to pay Ludwig a percentage of any sublicensing income, ranging from a low to mid-double digit percentage depending on various factors. During the year ended December 31, 2017, we paid a percentage of sublicensing income totaling \$2.0 million to Ludwig under the license agreements. No payments were made during the year ended December 31, 2018. The license agreements may each be terminated as follows: (i) by either party if the other party commits a material, uncured breach; (ii) by either party if the other party initiates bankruptcy, liquidation or similar proceedings; or (iii) by 4-AB or us (as applicable) for convenience upon 90 days' prior written notice. The license agreements also contain customary representations and warranties, mutual indemnification, confidentiality and arbitration provisions.

#### University of Connecticut Health Center

In May 2001, we entered into a license agreement with the University of Connecticut Health Center ("UConn") which was amended in March 2003 and June 2009. Through the license agreement, we obtained an exclusive, worldwide license to patent rights resulting from inventions discovered under a research agreement that was effective from February 1998 until December 2006. The term of the license agreement ends when the last of the licensed patents expires in 2028 or becomes no longer valid. UConn may terminate the agreement: (1) if, after 30 days written notice for breach, we continue to fail to make any payments due under the license agreement, or (2) we cease to carry on our business related to the patent rights or if we initiate or conduct actions in order to declare bankruptcy. We may terminate the agreement upon 90 days written notice. We are required to make royalty payments on any obligations created prior to the effective date of termination of the license agreement. Upon expiration or termination of the license agreement due to breach, we have the right to continue to manufacture and sell products covered under the license agreement which are considered to be works in progress for a period of six months. The license agreement contains aggregate milestone payments of approximately \$1.2 million for each product we develop covered by the licensed patent rights. These milestone payments are contingent upon regulatory filings, regulatory approvals, and commercial sales of products. We have also agreed to pay UConn a royalty on the net sales of products covered by the license agreement as well as annual license maintenance fees beginning in May 2006. Royalties otherwise due on the net sales of products covered by the license agreement may be credited against the annual license maintenance fee obligations. Under the March 2003 amendment, we agreed to pay UConn an upfront payment and to make future payments for each patent or patent application with respect to which we exercised our option under the research agreement. As of December 31, 2018, we had paid approximately \$1.0 million to UConn under the license agreement. The license agreement gives us complete discretion over the commercialization of products covered by the licensed patent rights but also requires us to use commercially reasonable diligent efforts to introduce commercial products within and outside the United States. If we fail to meet these diligence requirements, UConn may be able to terminate the license agreement.

#### Regulatory Compliance

Governmental authorities in the United States and other countries extensively regulate the pre-clinical and clinical testing, manufacturing, labeling, storage, record keeping, advertising, promotion, export, marketing and distribution, among other things, of our investigational product candidates. In the United States, the FDA under the Federal Food, Drug, and Cosmetic Act, the Public Health Service Act and other federal statutes and regulations, subject pharmaceutical products to rigorous review.

In order to obtain approval of a new product from the FDA, we must, among other requirements, submit proof of safety and efficacy as well as detailed information on the manufacture and composition of the product. In most cases, this proof entails extensive pre-clinical, clinical, and laboratory tests. Before approving a new drug or marketing application, the FDA may also conduct pre-licensing inspections of the company, its contract research organizations and/or its clinical trial sites to ensure that clinical, safety, quality control, and other regulated activities are compliant with Good Clinical Practices (“GCP”), or Good Laboratory Practices (“GLP”), for specific non-clinical toxicology studies. The FDA may also require confirmatory trials, post-marketing testing, and extra surveillance to monitor the effects of approved products, or place conditions on any approvals that could restrict the commercial applications of these products. Once approved, the labeling, advertising, promotion, marketing, and distribution of a drug or biologic product must be in compliance with FDA regulatory requirements.

In Phase 1 clinical trials, the sponsor tests the product in a small number of patients or healthy volunteers, primarily for safety at one or more doses. Phase 1 trials in cancer are often conducted with patients who have end-stage or metastatic cancer. In Phase 2, in addition to safety, the sponsor evaluates the efficacy of the product in a patient population somewhat larger than Phase 1 trials. Phase 3 trials typically involve additional testing for safety and clinical efficacy in an expanded population at geographically dispersed test sites. The FDA may order the temporary or permanent discontinuation of a clinical trial at any time.

The sponsor must submit to the FDA the results of pre-clinical and clinical testing, together with, among other things, detailed information on the manufacture and composition of the product, in the form of a new drug application (“NDA”), or in the case of

biologics, a BLA. In a process that can take a year or more, the FDA reviews this application and, when and if it decides that adequate data are available to show that the new compound is both safe and effective for a particular indication and that other applicable requirements have been met, approves the drug or biologic for marketing.

Whether or not we have obtained FDA approval, we must generally obtain approval of a product by comparable regulatory authorities of international jurisdictions prior to the commencement of marketing the product in those jurisdictions. We are also subject to cGMP, GCP, and GLP compliance obligations and are subject to inspection by international regulatory authorities. International requirements may in some circumstances be more rigorous than U.S. requirements and may require additional investment in manufacturing process development, non-clinical studies, clinical studies, and record-keeping that are not required for U.S. regulatory compliance or approval. The time required to obtain this approval may be longer or shorter than that required for FDA approval and can also require significant resources in time, money and labor.

Under the laws of the United States, the countries of the European Union and other nations, we and the institutions where we sponsor research are subject to obligations to ensure the protection of personal information of human subjects participating in our clinical trials. We have instituted procedures that we believe will enable us to comply with these requirements and the contractual requirements of our data sources. The laws and regulations in this area are evolving, and further regulation, if adopted, could affect the timing and the cost of future clinical development activities.

We are also subject to regulation under the Occupational Safety and Health Act, the Toxic Substances Control Act, the Resource Conservation and Recovery Act, and other current and potential future federal, state, or local regulations. Our research and development activities involve the controlled use of hazardous materials, chemicals, biological materials, various radioactive compounds, and for some experiments we use recombinant DNA. We believe that our procedures comply with the standards prescribed by local, state, and federal regulations; however, the risk of injury or accidental contamination cannot be completely eliminated. We conduct our activities in compliance with the National Institutes of Health Guidelines for Recombinant DNA Research.

Additionally, the U.S. Foreign Corrupt Practices Act (“FCPA”), prohibits U.S. corporations and their representatives from offering, promising, authorizing or making payments to any foreign government official, government staff member, political party or political candidate in an attempt to obtain or retain business abroad. The scope of the FCPA includes interactions with certain healthcare professionals in many countries. Other countries have enacted similar anti-corruption laws and/or regulations.

#### Competition

Competition in the pharmaceutical and biotechnology industries is intense. Many pharmaceutical or biotechnology companies have products on the market and are actively engaged in the research and development of products for the treatment of cancer.

Many competitors have substantially greater financial, manufacturing, marketing, sales, distribution, and technical resources, and more experience in research and development, clinical trials, and regulatory matters, than we do. Competing companies developing or acquiring rights to more efficacious therapeutic products for the same diseases we are targeting, or which offer significantly lower costs of treatment, could render our products noncompetitive or obsolete. See Part I-Item 1A. “Risk Factors-Risks Related to our Business-Our competitors may have superior products, manufacturing capability, selling and marketing expertise and/or financial and other resources.”

Academic institutions, governmental agencies, and other public and private research institutions conduct significant amounts of research in biotechnology, medicinal chemistry and pharmacology. These entities have become increasingly active in seeking patent protection and licensing revenues for their research results. They also compete with us in recruiting and retaining skilled scientific talent.

The CPM landscape is crowded with several competitors developing assets against a number of targets. Development plans are spread out across various indications and lines of therapy, either alone or in combination with other assets. Competitors range from small cap to large cap companies, with assets in pre-clinical or clinical stages of development. Therefore, the landscape is dynamic and constantly evolving. We and our partners have CPM antibody programs, currently in clinical stage development targeting PD-1, CTLA-4, GITR, OX40, TIM-3 and LAG-3. We are aware of many companies that have antibody-based products on the market or in clinical development that are directed to the same biological targets as these programs, including, without limitation, the following: (1) BMS markets ipilimumab, an anti-CTLA-4 antibody, and nivolumab, an anti-PD-1 antibody, and is developing additional antagonists to LAG-3 and TIM-3. BMS also has next generation anti-CTLA-4 antibodies in the clinic, which may be competitive to our next generation anti-CTLA-4 program, (2) Merck has an approved anti-PD-1 antibody, as well as anti-CTLA-4 and LAG-3 antagonists and an anti-GITR agonist in clinical development, (3) Regeneron has an approved anti-PD-1 antibody as well as antibodies targeting CTLA-4 and LAG-3 in preclinical or early clinical development, (4) AstraZeneca has an approved anti PD-L1 antibody, as well as an anti-CTLA-4 (using a different isotype, an IgG2 isotype) targeting antibody in the clinic, (5) Pfizer has an approved anti-PD-L1 (with Merck KgaA) as well as anti-PD-1, and anti-OX40 antibodies in clinical development, and (6) Roche/Genentech has an approved anti-PD-L1 antibody. Besides these PD-1 and PD-L1 antibodies that were approved in the U.S., we are also aware of competitors with approved PD-1 agents in ex-US geographies such as China. These include Innovent Biologics and Shanghai Junshi Biosciences. We are also aware of other competitors with PD-1/PD-L1 agents in clinical development, including but not limited to, AbbVie, Arcus



Biosciences, Boehringer Ingelheim, Tesaro, Beigene, Eli Lilly, Jiangsu HengRui Medicine, MacroGenics/Incyte, CytomX/BMS, Novartis, Symphogen, Jounce Therapeutics, Gilead Sciences, Janssen, CBT Pharmaceuticals/Genor Biopharma, Checkpoint Therapeutics, CStone Pharmaceuticals, Livzon MabPharm Inc, Suzhou Alphamab, Mabspace Biosciences, Henlix Biotech Inc., Akeso Biopharma and CSPC ZhongQi Pharmaceutical Technology. We are also aware of competitors with pre-clinical antibodies against PD-1 or PD-L1. In addition, we are aware of competitors with clinical stage antibodies against GITR, OX40, LAG-3, TIM-3 as well as our earlier stage programs such as TIGIT and CD137. As outlined above, some of these include, but are not limited to, BMS, Pfizer, Novartis, Merck, Tesaro, Regeneron, Eli Lilly, OncoMed, Boehringer Ingelheim, Potenza, Arcus Biosciences, GlaxoSmithKline, AbbVie, Leap Therapeutics and Symphogen. Additionally, we are aware of competitors developing preclinical assets and bispecifics against each of the above targets. There is no guarantee that our antibody product candidates will be able to compete with our competitors' antibody products and product candidates.

We are conducting both single arm and combination trials in second line cervical cancer. We are aware that Merck's PD-1 antagonist, Keytruda, has been approved in advanced cervical cancer. We are also aware of industry sponsored clinical trials, including exploratory studies that are underway in this setting. Clinical stage competitors include, but are not limited to, Regeneron (anti-PD-1), Ono Pharmaceuticals and BMS (anti-PD-1 alone or in combination with agents against other checkpoint targets), Seattle Genetics and Genmab (antibody drug conjugate targeting Tissue Factor), Iovance Biotherapeutics (autologous TILs), Genor Biopharma and Lee Pharmaceuticals. Additionally, we are aware of other early stage clinical trials testing alternate checkpoint targets in cervical cancer patients. These include, but are not limited to, OX40 +/- CD137 agonists (Pfizer) and anti-PD-1 + anti-ICOS (GSK/Merck).

We have autologous vaccine programs in development including our Prophage vaccine in clinical development for GBM. We are aware of other therapeutic options in GBM that could compete with our vaccine, including but not limited to the following: Merck markets temozolomide for treatment of patients with ndGBM and refractory astrocytoma. Other companies are developing vaccines for the treatment of patients with ndGBM, including, but not limited to Northwest Biotherapeutics (DC-Vax), Mimivax Inc. (SurVaxM) and Annias Immunotherapeutics (CMV Vaccine). Other companies may begin development programs as well. We are advancing our neoantigen vaccine, AutoSynVax, in solid tumors. There are companies advancing individualized or synthetic vaccine technologies and/or patient-specific medicine techniques that compete with our HSP based vaccines such as: Neon Therapeutics, Gritstone Oncology, Advaxis/Amgen, BioNTech, Moderna/Merck, Genocea Biosciences, ISA Pharmaceuticals, Nouscom, EpiVax Inc., and Vaccibody.

In addition, and prior to regulatory approval, if ever, our vaccines and our other product candidates may compete for access to patients with other products in clinical development, with products approved for use in the indications we are studying, or with off-label use of products in the indications we are studying. We anticipate that we will face increased competition in the future as new companies enter markets we seek to address and scientific developments surrounding immunotherapy and other traditional cancer therapies continue to accelerate.

We are aware of compounds that claim to be comparable to QS-21 Stimulon that are being used in clinical trials. Several other vaccine adjuvants are in development or in use and could compete with QS-21 Stimulon for inclusion in vaccines. These adjuvants may include but are not limited to: (1) oligonucleotides, under development by Pfizer, Idera, and Dynavax, (2) MF59, under development by Novartis, (3) IC31, under development by Intercell (now part of Valneva), and (4) MPL, under development by GSK. In the past, we have provided QS-21 Stimulon to other entities under materials transfer arrangements. In at least one instance, it is possible that this material was used unlawfully to develop synthetic formulations and/or derivatives of QS-21. In addition, companies such as Adjuvance Technologies, Inc., CSL Limited, and Novavax, Inc., as well as academic institutions and manufacturers of saponin extracts, are developing saponin adjuvants, including derivatives and synthetic formulations. These sources may be competitive to our ability to execute future partnering and licensing arrangements involving QS-21 Stimulon. The existence of products developed by these and other competitors, or other products of which we are not aware, or which other companies may develop in the future, may adversely affect the marketability of products developed or sold using QS-21 Stimulon.

We are also aware of a third party that manufactures pre-clinical material purporting to be comparable to QS-21 Stimulon. The claims being made by this third party may create marketplace confusion and have an adverse effect on the goodwill generated by us and our partners with respect to QS-21 Stimulon. We are also aware of at least two additional manufacturers of QS-21. Any diminution of this goodwill may have an adverse effect on our ability to commercialize future products, if any, incorporating this technology, either alone or with a third party.

#### Employees

As of February 28, 2019, we had 294 employees, of whom 90 were PhDs and three were MDs. None of our employees are subject to a collective bargaining agreement. We believe that we have good relations with our employees.

#### Corporate History

Antigenics L.L.C. was formed as a Delaware limited liability company in 1994 and was converted to Antigenics Inc., a Delaware corporation, in February 2000 in conjunction with our initial public offering of common stock. On January 6, 2011, we changed our name from Antigenics Inc. to Agenus Inc.

## Availability of Periodic SEC Reports

Our Internet website address is [www.agenusbio.com](http://www.agenusbio.com). We make available free of charge through our website our annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K, and amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended (“Exchange Act”), as soon as reasonably practicable after we electronically file such material with, or furnish such material to, the Securities and Exchange Commission (the “SEC”). The contents of our website are not part of, or incorporated into, this document. In addition, we regularly use our website to post information regarding our business, product development programs and governance, and we encourage investors to use our website, particularly the information in the sections entitled “Financial” and “News,” as sources of information about us.

The SEC maintains an Internet site that contains reports, proxy and information statements, and other information regarding issuers that file electronically with the SEC at [www.sec.gov](http://www.sec.gov).

The contents of the websites referred to above are not incorporated into this filing. Further, our references to the URLs for these websites are intended to be inactive textual references only.

## Item 1A. Risk Factors

Our future operating results could differ materially from the results described in this Annual Report on Form 10-K due to the risks and uncertainties described below. You should consider carefully the following information about risks below in evaluating our business. If any of the following risks actually occur, our business, financial conditions, results of operations and future growth prospects would likely be materially and adversely affected. In these circumstances, the market price of our common stock would likely decline.

We cannot assure investors that our assumptions and expectations will prove to be correct. Important factors could cause our actual results to differ materially from those indicated or implied by forward-looking statements. See “Note Regarding Forward-Looking Statements” in this Annual Report on Form 10-K. Factors that could cause or contribute to such differences include those factors discussed below.

### Risks Related to our Business

If we incur operating losses for longer than we expect, or we are not able to raise additional capital, we may be unable to continue our operations, or we may become insolvent.

Our net losses for the years ended December 31, 2018, 2017, and 2016, were \$162.0 million, \$120.7 million, and \$127.0 million, respectively. We expect to incur additional losses over the next several years as we continue to research and develop our technologies and pursue partnering opportunities, regulatory strategies, commercialization, and related activities. Furthermore, our ability to generate cash from operations is dependent on the success of our licensees and collaboration partners, as well as the likelihood and timing of new strategic licensing and partnering relationships and/or successful development and commercialization of product candidates, including through our antibody programs and platforms, our vaccine programs, and our saponin-based vaccine adjuvants.

On December 31, 2018, we had \$53.1 million in cash and cash equivalents. We believe that, based on our current plans and activities, including \$150.0 million of additional funding we received in connection with our transactions with Gilead subsequent to December 31, 2018, our cash on-hand will be sufficient to satisfy our liquidity requirements for more than one year from when these financial statements were issued.

To date, we have financed our operations primarily through the sale of equity and debt securities. In order to finance future operations, we will be required to raise additional funds in the capital markets, through arrangements with collaboration partners or from other sources. Additional financing may not be available on favorable terms, or at all. If we are unable to raise additional funds when we need them or if we incur operating losses for longer than we expect, we may not be able to continue some or all of our operations, or we may become insolvent. We also may be forced to license or sell technologies to others under agreements that are on unfavorable terms or allocate to third parties substantial portions of the potential value of these technologies.

There are a number of factors that will influence our future capital requirements, including, without limitation, the following:

- the number and characteristics of the product candidates we and our partners pursue;
  - our and our partners' ability to successfully develop, manufacture, and commercialize product candidates;
- the scope, progress, results and costs of researching and developing our future product candidates and conducting pre-clinical and clinical trials;

- the timing of, and the costs involved in, obtaining regulatory approvals for our and our licensees' product candidates;
- the cost of manufacturing;
- our ability to establish and maintain strategic partnerships, licensing or other arrangements and the financial terms of such arrangements;
- the costs involved in preparing, filing, prosecuting, maintaining, defending and enforcing our intellectual property rights;
- the costs associated with any successful commercial operations; and
- the timing, receipt and amount of sales of, or royalties on, our future products and those of our partners, if any.

General economic conditions in the United States economy and abroad may have a material adverse effect on our liquidity and financial condition, particularly if our ability to raise additional funds is impaired. The ability of potential patients and/or health care payers to pay for our future products, if any, could also be adversely impacted, thereby limiting our potential revenue. In addition, any negative impacts from any deterioration in the credit markets on our collaboration partners could limit potential revenue from our product candidates.

Our obligations to HCR and the holders of our 2015 Subordinated Notes could materially and adversely affect our liquidity.

In January 2018, we and our wholly-owned subsidiary, Antigenics LLC ("Antigenics"), entered into a Royalty Purchase Agreement with HCR, pursuant to which HCR purchased 100% of Antigenics' worldwide rights to receive royalties from GSK on sales of GSK's vaccines containing our QS-21 Stimulon adjuvant. As consideration for the purchase of the royalty rights, HCR paid \$190.0 million at closing, less certain transaction expenses. Of the closing proceeds, approximately \$161.9 million was used to redeem Antigenics' \$115.0 million principal amount of notes issued pursuant to the Note Purchase Agreement with Oberland Capital SA Zermatt LLC, and we retained approximately \$28.0 million of net proceeds. Antigenics is also entitled to receive up to \$40.35 million in milestone payments based on sales of GSK's vaccines as follows: (i) \$15.1 million upon reaching \$2.0 billion last-twelve-months net sales any time prior to 2024 and (ii) \$25.25 million upon reaching \$2.75 billion last-twelve-months net sales any time prior to 2026. Antigenics will owe approximately \$25.9 million to HCR in 2021 if neither of the following sales milestones are achieved: (i) 2019 sales of GSK's vaccines exceed \$1.0 billion or (ii) 2020 sales of GSK's vaccines exceed \$1.75 billion (the "Rebate Payment"). As part of the transaction, we provided a guaranty for the potential Rebate Payment and secured the obligation with substantially all of our assets pursuant to a security agreement. If GSK's sales do not achieve either of the relevant milestones and we are obligated to make the Rebate Payment, our liquidity could be materially and adversely affected.

In February 2015, we exchanged senior subordinated promissory notes that we issued in 2013 for new senior subordinated promissory notes in the aggregate principal amount of \$5.0 million with annual interest at 8%, and we issued an additional \$9.0 million principal amount of such notes (the "2015 Subordinated Notes"). The 2015 Subordinated Notes were originally due February 2018, and in March 2017, we amended the 2015 Subordinate Notes to extend the maturity date to February 2020. The 2015 Subordinated Notes include default provisions that allow for the acceleration of the principal payment of the 2015 Subordinated Notes in the event we become involved in certain bankruptcy proceedings, become insolvent, fail to make a payment of principal or (after a grace period) interest on the 2015 Subordinated Notes, default on other indebtedness with an aggregate principal balance of \$13.5 million or more if such default has the effect of accelerating the maturity of such indebtedness, or become subject to a legal judgment or similar order for the payment of money in an amount greater than \$13.5 million if such amount will not be covered by third-party insurance. If we default on the 2015 Subordinated Notes and the repayment of such indebtedness is accelerated, our liquidity could be materially and adversely affected.

If we do not have sufficient cash on hand to pay the Rebate Payment when due, or to otherwise service our 2015 Subordinated Notes, we may be required, among other things, to:

- seek additional financing in the debt or equity markets;
- refinance or restructure all or a portion of our indebtedness;

sell, out-license, or otherwise dispose of assets; and/or

reduce or delay planned expenditures on research and development and/or commercialization activities.

Such measures might not be sufficient to enable us to make principal and interest payments. In addition, any such financing, refinancing, or sale of assets might not be available on favorable terms, if at all.

Our AGEN2034 and AGEN1884 antibody programs are in potential registrational studies, and there is no guarantee that we will be successful in advancing these through clinical development on our desired timeline, if at all, or that we will be able to commercialize them successfully.

Our anti-PD-1 and anti-CTLA-4 programs (AGEN2034 and AGEN1884, respectively) are in clinical trials that included a Phase 1 dose escalation with expansion cohorts in multiple solid tumors. These molecules are now in expansion trials with both anti-PD-1 monotherapy and anti-PD-1 and anti-CTLA-4 combination trials for patients with second-line cervical cancer that are designed to support one or more Biologic License Application (“BLA”) filings as soon as 2020. If approved, we intend to commercialize these assets in 2021. These timelines are aggressive and subject to various factors outside of our control, including patient accrual rates for our clinical trials. If our trials are unable to accrue patients at the rate we expect, we are unlikely to hit our anticipated timelines and our business and financial prospects could be materially adversely affected. In addition, in order to file a BLA and seek accelerated approval, we must also launch a confirmatory trial and have it be substantially underway at that time. We have not yet initiated a confirmatory trial. There is no guarantee that we will be able to file a BLA in 2020, if at all.

We have previously presented early data on these programs at major oncology conferences that demonstrated a clinical benefit (i.e., complete response, partial response or disease stabilization) in more than 60% of patients treated with AGEN1884 and AGEN2034. Even though we have observed positive results to date, they may not necessarily be predictive of the final results of the trials or future clinical trials. Many companies in the pharmaceutical, biopharmaceutical and biotechnology industries have suffered significant setbacks in clinical trials after achieving positive results, and we cannot be certain that we will not face similar setbacks.

Even if AGEN2034 and/or AGEN1884 are approved, there is no guarantee that we will be able to successfully commercialize them or penetrate any commercial markets. We are initially targeting cervical cancer, which is a small subset of the overall market. We intend to use proceeds from our sales of any Biotech Electronic Security Tokens to expand the development and commercial potential of AGEN2034, but there is no guarantee that we will sell sufficient tokens, if any, to do so. See “Risk Factors—Risks Relating to Our Tokens—There is no assurance that we will sell a sufficient number of tokens, if any, to meet our business or financial goals.”

Our other antibody programs are in early stage development, and there is no guarantee that we or our partners will be successful in advancing antibody product candidates into and through clinical development.

Our additional antibody programs are currently in early stage development, and many of our antibody programs are pre-clinical. Even if our pre-clinical studies or our and/or our partners’ clinical trials produce positive results, they may not necessarily be predictive of the results of future clinical trials. Many companies in the pharmaceutical, biopharmaceutical and biotechnology industries have suffered significant setbacks in clinical trials after achieving positive results in pre-clinical development or earlier clinical trials, and we cannot be certain that we will not face similar setbacks. These setbacks have been caused by, among other things, pre-clinical findings made while clinical trials were underway or safety or efficacy observations made in clinical trials, including adverse events. Moreover, pre-clinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that believed their product candidates performed satisfactorily in pre-clinical studies and clinical trials nonetheless failed to obtain regulatory approval. If we and our partners fail to produce positive results in clinical trials of antibodies, our business and financial prospects would be materially adversely affected.

Although we are striving to file a number of INDs to advance novel antibodies, cell therapy candidates, and neoantigen vaccine combinations into the clinic, there is no guarantee that we will be able to do so on that timeline, if at all. Our stated timelines are aggressive and subject to various risks, including resource constraints. If we are unable to advance novel candidates into the clinic as planned due to resource constraints or otherwise, our business and partnering prospects could be materially adversely affected.

We have undergone significant growth across multiple locations over the past few years, and are focusing on further enhancing core areas and capabilities as we move toward commercialization. In addition, we have consolidated certain sites while expanding others to focus on our core priorities and future needs. We may encounter difficulties in managing these growth and/or consolidation efforts, either of which could disrupt our operations.

Since our acquisition of Agenus Switzerland Inc., formerly known as 4-Antibody AG (“4-AB”) in February 2014, we have more than tripled our headcount, in part through various acquisitions and the expansion of our research and development activities both nationally and internationally. While we have restructured our organization over the past few years, we expect to continue increasing our headcount in certain core areas as we continue to build our development, manufacturing and commercialization capabilities and integrate our acquired technology platforms. To manage these organizational changes, we must continue to implement and improve our managerial, operational and financial systems and continue to recruit, train and retain qualified personnel. If our management is unable to effectively manage our growth, our expenses may increase more than expected, our timelines may be delayed, our ability to generate revenue could be reduced, and we may not be able to implement our business strategy.



As part of our efforts to optimize efficiency across our organization, we closed our Jena, Germany office in 2016 and consolidated these operations in the United Kingdom and Switzerland. In 2017, we completed a reduction in force in our Lexington, MA facility, which included certain members of our management, in line with our prioritization efforts, and we closed our office in Basel, Switzerland and transferred our research and development assets and capabilities there to the United Kingdom. If these transition efforts prove to be unsuccessful, or if we identify management or operational gaps in connection with our changes, it could cause delays in discovery timelines and increased costs for certain of our internal and partnered programs, which also could have an adverse effect on our business, financial condition and results of operations. We are still in the process of liquidating 4-AB and transferring intellectual property rights from Switzerland to the United States or elsewhere. There could be adverse tax consequences resulting from this migration of intellectual property rights, which could have an adverse effect on our business and operations.

Our synthetic Heat Shock Protein (“HSP”) peptide-based platform is in early stage development, and there is no guarantee that a product candidate will progress from this platform.

In June 2014, we reported positive results from a Phase 2 trial with HerpV<sup>TM</sup>, a vaccine candidate for genital herpes from our synthetic HSP peptide-based platform. The Phase 2 trial met its formal endpoints, subjects were not followed long enough to determine whether the magnitude of the effect on viral load would be sufficient to significantly reduce the incidence, severity, or duration of herpetic lesions or reduce the risk of viral transmission. Although we have not advanced this program into a Phase 3 trial, we initiated our ASV synthetic cancer vaccine program based on our prior findings with this platform. We initiated our first clinical trial for our first AutoSynVax product candidate in 2017 and reported safety and immunogenicity of the vaccine at CIMT2018. Although we are planning to initiate a combination trial with ASV and one or more of our antibodies, the timeline is uncertain and there is no guarantee that we will be able to do so at all. Furthermore, it is possible that research and discoveries by others will render any product candidate from this platform as obsolete or noncompetitive.

We may not be able to advance clinical development or commercialize our cancer vaccine candidates or realize any benefits from these programs.

The probability of future clinical development efforts leading to marketing approval and commercialization of Prophage vaccines is highly uncertain. Prophage vaccines have been in clinical development for over 16 years, including multiple Phase 1 and 2 trials in eight different tumor types as well as randomized Phase 3 trials in metastatic melanoma and adjuvant renal cell carcinoma. To date, the only marketing approval for Prophage is in Russia where commercialization of the approved product was unsuccessful. All of our currently planned trials involving Prophage are intended to be sponsored by third parties, and there is no guarantee that they will occur at all.

Our current clinical trial plans with Prophage vaccines entail one government sponsored IND in which we provide support and product supply. For third-party sponsored trials, we lack the ability to control trial design, timelines, tumor tissue procurement and data availability. For example, in January 2017, we announced a clinical trial collaboration with the National Cancer Institute (“NCI”), whereby the NCI is conducting a double-blind, randomized controlled Phase 2 trial to evaluate the effect of Prophage vaccine in conjunction with Merck’s pembrolizumab on the overall survival rate of patients with newly diagnosed glioblastoma (“ndGBM”). In addition, the Phase 2 trial of Prophage vaccine in combination with bevacizumab in patients with surgically resectable recurrent glioma that was being conducted under the sponsorship of the Alliance for Clinical Trials in Oncology, a cooperative group of the NCI, has been closed. Our other cancer vaccine programs (ASV and PSV) are in Phase 1 and pre-clinical development, respectively, and there is no guarantee that they will successfully advance in and through the clinic. ASV also utilizes QS-21 Stimulon, and any inability or delay in securing adequate supplies of the adjuvant could have an adverse impact on the program or otherwise delay timelines. Current and future studies may eventually be terminated due to, among other things, slow enrollment, lack of probability that they will yield useful translational and/or efficacy data, lengthy timelines, or the unlikelihood that results will support timely or successful regulatory filings.

Changes in our manufacturing strategies, manufacturing problems, or increased demand may cause delays, unanticipated costs, or loss of revenue streams within or across our programs.

Our antibody programs will require substantial manufacturing development and investment to progress. We are currently progressing a portfolio of antibody programs that are at different stages of development. If these efforts are delayed or do not produce the desired outcomes, this will cause delays in development timelines and increased costs, which may cause us to limit the size and scope of our efforts and studies. In 2015, we secured our own antibody manufacturing capabilities with the purchase of a manufacturing pilot plant from XOMA Corporation (“XOMA”), and we expect this facility to supply us with antibody drug substance requirements through clinical proof-of-concept studies. We will also need to develop or secure later phase and/or commercial manufacturing capabilities for larger, registrational studies or any commercial supply requirements. For the programs for which we will produce our own drug substance, we will continue to rely on third parties for fill-finish services and other parts of the manufacturing process. These services include the storage and maintenance of our drug substance during all stages of the

manufacturing process. While we maintain insurance to cover certain potential losses, there is no guarantee that our insurance coverage will be adequate. Furthermore, we currently rely on contract manufacturing organizations (“CMOs”) and contract research organizations (“CROs”) to support some of our existing antibody programs. Our dependence on external CMOs for the manufacture of certain antibodies results in intrinsic risks to our performance, timelines, and costs of our accelerated development plans, and which could divert resources away from our antibody programs and/or lead to delays in the development of our product candidates. In the event that our antibody programs require progressively larger production capabilities, our options for qualified CMOs may become more limited.

To date, we have manufactured our Prophage vaccines in our Lexington, MA facility. Manufacturing of the Prophage vaccines is complex, and various factors could cause delays or an inability to supply the vaccine. Deviations in the processes controlling manufacture or deficiencies in size or quality of source material could result in production failures. Specific vulnerabilities in the process may exist in tumor types in which quality or quantity of tissue is limited. In addition, regulatory bodies may require us to make our manufacturing facility a single product facility. In such an instance, we would no longer have the ability to manufacture Prophage vaccines in addition to other product candidates in our current facility.

We have given our corporate QS-21 Stimulon licensee, GSK, manufacturing rights for QS-21 Stimulon for use in their product programs. We have retained the right to manufacture QS-21 for ourselves and third parties, although no other such programs are anticipated to bring us substantial revenues in the near future, if ever. Although we have the right to secure certain quantities of QS-21 from GSK and we have some internal supply in-house, we currently do not have an alternative long-term supply partner for this adjuvant.

Our ability to efficiently manufacture our product candidates is contingent, in part, upon our own, and our CMOs’, ability to ramp up production in a timely manner without the benefit of years of experience and familiarity with the processes, which we may not be able to adequately transfer. We currently rely upon and expect to continue to rely upon third parties, potentially including our collaborators or licensees, to produce materials required to support our product candidates, pre-clinical studies, clinical trials, and any future commercial efforts. A number of factors could cause production interruptions at either our manufacturing facility or the facilities of our CMOs or suppliers, including equipment malfunctions, labor or employment retention problems, natural disasters, power outages, terrorist activities, or disruptions in the operations of our suppliers. Alternatively, there is the possibility we may have excess manufacturing capacity if product candidates do not progress as planned.

As mentioned above, reliance on third-party manufacturers entails risks to which we would not be subject if we manufactured all of our product candidates ourselves, including reliance on the third party for regulatory compliance, the possibility of breach of the manufacturing agreement by the third party because of factors beyond our control, and the possibility of termination or non-renewal of the agreement by the third party, based on its own business priorities, at a time that is costly or inconvenient for us.

Biopharmaceutical manufacturing is also subject to extensive government regulation. Components of a finished therapeutic product approved for commercial sale or used in late-stage clinical trials must be manufactured in accordance with current good manufacturing practices. These regulations govern manufacturing processes and procedures (including record-keeping) and the implementation and operation of quality systems to control and assure the quality of investigational products and products approved for sale. Our facilities and quality systems and the facilities and quality systems of some or all of our third-party contractors must pass a pre-approval inspection for compliance with the applicable regulations as a condition of regulatory approval of a product candidate. In addition, facilities are subject to on-going inspections and routine audits, and minor changes in manufacturing processes may require additional regulatory approvals and audits, either of which could cause us to incur significant additional costs, set-backs or delays and eventual loss of revenue.

Risks associated with doing business internationally could negatively affect our business.

We currently have research and development operations in the United Kingdom, and we expect to pursue pathways to develop and commercialize our product candidates in both U.S. and non-U.S. jurisdictions. Various risks associated with foreign operations may impact our success. Possible risks of foreign operations include fluctuations in the value of foreign and domestic currencies, requirements to comply with various jurisdictional requirements such as data privacy regulations, disruptions in the import, export, and transportation of patient tumors and our products or product candidates, the product and service needs of foreign customers, difficulties in building and managing foreign relationships, the performance of our licensees or collaborators, geopolitical instability, unexpected regulatory, economic, or political changes in foreign and domestic markets, including without limitation any resulting from the United Kingdom's withdrawal from the European Union or our current political regime, and limitations on the flexibility of our operations and costs imposed by local labor laws.

Our competitors may have superior products, manufacturing capability, selling and marketing expertise and/or financial and other resources.

Our product candidates and the product candidates in development by our collaboration partners may fail because of competition from major pharmaceutical companies and specialized biotechnology companies that market products, or that are engaged in the development of product candidates and for the treatment cancer. Many of our competitors, including large pharmaceutical companies, have greater financial and human resources and more experience than we do. Our competitors may:

- develop safer or more effective therapeutic drugs or therapeutic vaccines and other products;
- establish superior intellectual property positions;
- discover technologies that may result in medical insights or breakthroughs, which render our drugs or vaccines obsolete, possibly before they generate any revenue, if ever;
- adversely affect our ability to recruit patients for our clinical trials;
- solidify partnerships or strategic acquisitions that may increase the competitive landscape;
  - develop or commercialize their product candidates sooner than we commercialize our own, if ever; or
- implement more effective approaches to sales and marketing and capture some of our potential market share.

There is no guarantee that our product candidates will be able to compete with potential future products being developed by our competitors.

The CPM landscape is crowded with several competitors developing assets against a number of targets. Development plans are spread out across various indications and lines of therapy, either alone or in combination with other assets. Competitors range from small cap to large cap companies, with assets in pre-clinical or clinical stages of development. Therefore, the landscape is dynamic and constantly evolving. We and our partners have CPM antibody programs, currently in clinical stage development targeting PD-1, CTLA-4, GITR, OX40, TIM-3 and LAG-3. We are aware of many companies that have antibody-based products on the market or in clinical development that are directed to the same biological targets as these programs, including, without limitation, the following: (1) BMS markets ipilimumab, an anti-CTLA-4 antibody, and nivolumab, an anti-PD-1 antibody, and is developing additional antagonists to LAG-3 and TIM-3. BMS also has next generation anti-CTLA-4 antibodies in the clinic, which may be competitive to our next generation anti-CTLA-4 program, (2) Merck has an approved anti-PD-1 antibody, as well as anti-CTLA-4 and LAG-3 antagonists and an anti-GITR agonist in clinical development, (3) Regeneron has an approved anti-PD-1 antibody as well as antibodies targeting CTLA-4 and LAG-3 in clinical development, (4) AstraZeneca has an approved anti PD-L1 antibody, as well as an anti-CTLA-4 targeting antibody in the clinic, (5) Pfizer has an approved anti-PD-L1 (with Merck KgaA) as well as anti-PD-1, and anti-OX40 antibodies in clinical development, and (6) Roche/Genentech has an approved anti-PD-L1 antibody. Besides these PD-1 and PD-L1 antibodies that were approved in the U.S., we are also aware of competitors with approved PD-1 agents in ex-U.S. geographies such as China. These include Innovent Biologics and Shanghai Junshi Biosciences. We are also aware of other competitors with PD-1/PD-L1 agents in clinical development, including but not limited to AbbVie, Arcus Biosciences, Boehringer Ingelheim, Tesaro, Beigene, Eli Lilly, Jiangsu HengRui Medicine, MacroGenics/Incyte, CytomX/BMS, Novartis, Symphogen, Jounce Therapeutics, Gilead Sciences, Janssen, CBT Pharmaceuticals/Genor Biopharma, Checkpoint Therapeutics, CStone Pharmaceuticals, Livzon MabPharm Inc, Suzhou Alphamab, Mabspace Biosciences, Henlix Biotech Inc., Akeso Biopharma and CSPC ZhongQi Pharmaceutical Technology. We are also aware of competitors with pre-clinical antibodies against PD-1 or PD-L1. In addition, we are aware of competitors with clinical stage antibodies against GITR, OX40, LAG-3, TIM-3 as well as our earlier stage programs such as TIGIT and CD137. As outlined above, some of these include, but are not limited to, BMS, Pfizer, Novartis, Merck, Tesaro, Regeneron, Eli Lilly, OncoMed, Boehringer Ingelheim, Potenza, Arcus Biosciences, GlaxoSmithKline, AbbVie, Leap Therapeutics and Symphogen. Additionally, we are aware of competitors developing preclinical assets and bispecifics against each of the above targets. There is no guarantee that our antibody product candidates will be able to compete with our competitors' antibody products and product candidates.

We are conducting both single arm and combination trials in second line cervical cancer. We are aware that Merck's PD-1 antagonist, Keytruda, has been approved in advanced cervical cancer. We are also aware of industry sponsored clinical trials, including exploratory studies, that are underway in this setting. Clinical stage competitors include, but are not limited to, Regeneron (anti-PD-1), Ono Pharmaceuticals and BMS (anti-PD-1 alone or in combination with agents against other checkpoint targets), Seattle Genetics and Genmab (antibody drug conjugate targeting Tissue Factor), Iovance Biotherapeutics (autologous TILs), Genor Biopharma and Lee Pharmaceuticals. Additionally, we are aware of other early stage clinical trials testing alternate checkpoint targets in cervical cancer patients. These include, but are not limited to, OX40 +/- CD137 agonists (Pfizer) and anti-PD-1 + anti-ICOS (GSK/Merck).

We have autologous vaccine programs in development including our Prophage vaccine in clinical development for GBM. We are aware of other therapeutic options in GBM that could compete with our vaccine, including but not limited to the following: Merck

markets temozolomide for treatment of patients with ndGBM and refractory astrocytoma. Other companies are developing vaccines for the treatment of patients with ndGBM, including, but not limited to, Northwest Biotherapeutics (DC-Vax), Mimivax Inc. (SurVaxM) and Annias Immunotherapeutics (CMV Vaccine). Other companies may begin development programs as well. We are advancing our neoantigen vaccine, AutoSynVax, in solid tumors. There are companies advancing individualized or synthetic vaccine technologies and/or patient-specific medicine techniques that compete with our HSP based vaccines such as: Neon Therapeutics, Gritstone Oncology, Advaxis/Amgen, BioNTech, Moderna/Merck, Genocea Biosciences, ISA Pharmaceuticals, Nouscom, EpiVax Inc., and Vaccibody.

In addition, and prior to regulatory approval, if ever, our vaccines and our other product candidates may compete for access to patients with other products in clinical development, with products approved for use in the indications we are studying, or with off-label use of products in the indications we are studying. We anticipate that we will face increased competition in the future as new companies enter markets we seek to address and scientific developments surrounding immunotherapy and other traditional cancer therapies continue to accelerate.

We are aware of compounds that claim to be comparable to QS-21 Stimulon that are being used in clinical trials. Several other vaccine adjuvants are in development or in use and could compete with QS-21 Stimulon for inclusion in vaccines. These adjuvants may include but are not limited to: (1) oligonucleotides, under development by Pfizer, Idera, and Dynavax, (2) MF59, under development by Novartis, (3) IC31, under development by Intercell (now part of Valneva), and (4) MPL, under development by GSK. In the past, we have provided QS-21 Stimulon to other entities under materials transfer arrangements. In at least one instance, it is possible that this material was used unlawfully to develop synthetic formulations and/or derivatives of QS-21. In addition, companies such as Adjuvance Technologies, Inc., CSL Limited, and Novavax, Inc., as well as academic institutions and manufacturers of saponin extracts, are developing saponin adjuvants, including derivatives and synthetic formulations. These sources may be competitive to our ability to execute future partnering and licensing arrangements involving QS-21 Stimulon. The existence of products developed by these and other competitors, or other products of which we are not aware, or which other companies may develop in the future, may adversely affect the marketability of products developed or sold using QS-21 Stimulon.

We are also aware of a third party that manufactures pre-clinical material purporting to be comparable to QS-21 Stimulon. The claims being made by this third party may create marketplace confusion and have an adverse effect on the goodwill generated by us and our partners with respect to QS-21 Stimulon. We are also aware of at least two additional manufacturers of QS-21. Any diminution of this goodwill may have an adverse effect on our ability to commercialize future products, if any, incorporating this technology, either alone or with a third party.

Failure to realize the anticipated benefits of our strategic acquisitions and licensing transactions could adversely affect our business, operations and financial condition.

An important part of our business strategy has been to identify and advance a pipeline of product candidates by acquiring and in-licensing product candidates, technologies and businesses that we believe are a strategic fit with our existing business. Since we acquired 4-AB in 2014, we have completed numerous additional strategic acquisitions and licensing transactions. The ultimate success of these strategic transactions entails numerous operational and financial risks, including:

- higher than expected development and integration costs;
- difficulty in combining the technologies, operations and personnel of acquired businesses with our technologies, operations and personnel;
- exposure to unknown liabilities;
- difficulty or inability to form a unified corporate culture across multiple office sites both nationally and internationally;
- inability to retain key employees of acquired businesses;

• disruption of our business and diversion of our management's time and attention; and  
• difficulty or inability to secure financing to fund development activities for such acquired or in-licensed product candidates, technologies or businesses.

We have limited resources to integrate acquired and in-licensed product candidates, technologies and businesses into our current infrastructure, and we may fail to realize the anticipated benefits of our strategic transactions. Any such failure could have an adverse effect on our business, operations and financial condition.



Failure to enter into and/or maintain significant licensing, distribution and/or collaboration agreements in a timely manner and on favorable terms to us may hinder or cause us to cease our efforts to develop and commercialize our product candidates, increase our development timelines, and/or increase our need to rely on partnering or financing mechanisms, such as sales of debt or equity securities, to fund our operations and continue our current and anticipated programs.

As previously noted, our ability to advance our antibody programs depends in part on collaboration agreements such as our collaborations with Gilead and Incyte. In addition, from time to time we engage in efforts to enter into licensing, distribution and/or collaboration agreements with one or more pharmaceutical or biotechnology companies to assist us with development and/or commercialization of our other product candidates. If we are successful in entering into such agreements, we may not be able to negotiate agreements with economic terms similar to those negotiated by other companies. We may not, for example, obtain significant upfront payments, substantial royalty rates or milestones. If we fail to enter into any such agreements in a timely manner or at all, our efforts to develop and/or commercialize our product candidates may be undermined. In addition, if we do not raise funds through any such agreements, we will need to rely on other financing mechanisms, such as sales of debt or equity securities, to fund our operations. Such financing mechanisms, if available, may not be sufficient or timely enough to advance our programs forward in a meaningful way in the short-term.

Because we rely on collaborators and licensees for the development and commercialization of certain of our product candidate programs, these programs may not prove successful, and/or we may not receive significant payments from such parties.

Part of our strategy is to develop and commercialize many of our product candidates by continuing or entering into arrangements with academic, government, or corporate collaborators and licensees. Our success depends on our ability to negotiate such agreements on favorable terms and on the success of the other parties in performing research, pre-clinical and clinical testing, completing regulatory applications, and commercializing product candidates. Our research, development, and commercialization efforts with respect to antibody candidates from our technology platforms are, in part, contingent upon the participation of institutional and corporate collaborators. For example, in February 2015, we began a broad collaboration with Incyte to pursue the discovery and development of antibodies, and in December 2018 we entered into a partnership with Gilead relating to five of our antibody programs. Furthermore, we have a collaboration arrangement with Recepta for CTLA-4 and PD-1, giving Recepta rights to certain South American countries and requiring us to agree upon development plans for these product candidates. Disagreements or the failure of either party to perform satisfactorily could have an adverse impact on these programs.

The Brain Tumor Trials Collaborative, through the NCI, is sponsoring a Phase 2 clinical trial of our Prophage vaccine candidate in combination with Merck's pembrolizumab in patients with glioma. When our licensees or third-party collaborators sponsor clinical trials using our product candidates, we cannot control the timing of enrollment, data readout, or quality of such trials or related activities.

Development activities for our collaboration programs may fail to produce marketable products due to unsuccessful results or abandonment of these programs, failure to enter into future collaborations or license agreements, or the inability to manufacture product supply requirements for our collaborators and licensees. Several of our agreements also require us to transfer important rights and regulatory compliance responsibilities to our collaborators and licensees. As a result of these collaboration agreements, we will not control the nature, timing, or cost of bringing these product candidates to market. Our collaborators and licensees could choose not to, or be unable to, devote resources to these arrangements or adhere to required timelines, or, under certain circumstances, may terminate these arrangements early. They may cease pursuing product candidates or elect to collaborate with different companies. In addition, these collaborators and licensees, outside of their arrangements with us, may develop technologies or products that are competitive with those that we are developing. From time to time, we may also become involved in disputes with our collaborators or licensees. Such disputes could result in the incurrence of significant expense, or the termination of collaborations. We may be unable to fulfill all of our obligations to our collaborators, which may result

in the termination of collaborations. As a result of these factors, our strategic collaborations may not yield revenue. Furthermore, we may not be able to enter into new collaborations on favorable terms or at all. Failure to generate significant revenue from collaborations could increase our need to fund our operations through sales of debt or equity securities and would negatively affect our business prospects.

Our internal computer systems, or those of our third-party CROs, CMOs, licensees, collaborators or other contractors or consultants, may fail or suffer security breaches, which could result in a material disruption in our business and operations or could subject us to sanctions and penalties that could have a material adverse effect on our reputation or financial condition.

Despite the implementation of security measures, our internal computer systems and those of our current and future CROs, CMOs, licensees, collaborators and other contractors and consultants are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. Potential vulnerabilities can also be exploited from inadvertent or intentional actions of our employees, third-party vendors, business partners, or by malicious third parties. Attacks of this nature are increasing in their frequency, levels of persistence, sophistication and intensity, and are being conducted by sophisticated and organized groups and individuals with a wide range of motives (including, but not limited to, industrial espionage)

and expertise, including organized criminal groups, “hacktivists,” nation states and others. In addition to the extraction of sensitive information, such attacks could include the deployment of harmful malware, ransomware, denial-of-service attacks, social engineering and other means to affect service reliability and threaten the confidentiality, integrity and availability of information. In addition, the prevalent use of mobile devices increases the risk of data security incidents. While we are not aware of any such material system failure, accident or security breach to date, if such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our development programs and our business operations. For example, the loss of clinical trial data from completed, on-going or future clinical trials could result in delays in our regulatory approval efforts and significant costs to recover or reproduce the data. Likewise, we rely on third parties to manufacture certain of our drug candidates and conduct clinical trials, and similar events relating to their computer systems could also have a material adverse effect on our business. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liabilities and the further development and commercialization of our product candidates could be delayed. We do not maintain cyber liability insurance, and would therefore have no coverage for any losses resulting from any data security incident.

We use and store customer, vendor, employee and business partner and, in certain instances patient, personally identifiable information in the ordinary course of our business. We are subject to various domestic and international privacy and security regulations, including but not limited to the Health Insurance Portability and Accountability Act of 1996 (“HIPAA”), which mandates, among other things, the adoption of uniform standards for the electronic exchange of information in common healthcare transactions, as well as standards relating to the privacy and security of individually identifiable health information, which require the adoption of administrative, physical and technical safeguards to protect such information. In addition, many states have enacted comparable laws addressing the privacy and security of health information, some of which are more stringent than HIPAA. Failure to comply with these standards, or a computer security breach or cyber-attack that affects our systems or results in the unauthorized release of proprietary or personally identifiable information, could subject us to criminal penalties and civil sanctions, and our reputation could be materially damaged, and our operations could be impaired. We may also be exposed to a risk of loss or litigation and potential liability, which could have a material adverse effect on our business, results of operations and financial condition.

We are highly reliant on certain members of our management team. In addition, we have limited internal resources and if we fail to recruit and/or retain the services of key employees and external consultants as needed, we may not be able to achieve our strategic and operational objectives.

Garo H. Armen, Ph.D., the Chairman of our Board of Directors and our Chief Executive Officer who co-founded the Company in 1994, is integral to building our company and developing our technology. If Dr. Armen is unable or unwilling to continue his relationship with Agenus, our business may be adversely impacted. We have an employment agreement with Dr. Armen, and he plays an important role in our day-to-day activities. We do not carry a key employee insurance policy for Dr. Armen or any other employee.

Our future growth success depends to a significant extent on the skills, experience and efforts of our executive officers and key members of our clinical and scientific staff. We face intense competition for qualified individuals from other pharmaceutical, biopharmaceutical and biotechnology companies, as well as academic and other research institutions. We may be unable to retain our current personnel or attract or assimilate other highly qualified management and clinical personnel in the future on acceptable terms. The loss of any or all of these individuals could harm our business and could impair our ability to support our collaboration partners or our growth generally. If our management is unable to effectively manage our growth, our expenses may increase more than expected, our ability to generate revenue could be reduced and we may not be able to implement our business strategy.

We intend to advance our cell therapy business through our subsidiary, AgenTus Therapeutics, eventually with separate funding. Moving intellectual property assets into AgenTus Therapeutics in foreign jurisdictions could have adverse tax consequences, and there is no guarantee that we will be able to attract external funding. Moreover, even if

the business is funded, there is no guarantee that it will be successful.

We are currently in the process of pursuing external funding and partnership opportunities to advance AgenTus Therapeutics, but Agenus is currently funding such operations. There is no guarantee that external funding will be available. If funding is available, there is no guarantee that it will be on attractive or acceptable terms, or that it will be adequate to advance the business to an inflection point for additional funding, including any potential initial public offering. Similarly, there is no guarantee that partnership opportunities will be available on attractive terms, if at all. If external funding is not available, we may be forced to either retire these programs or continue to use internal resources to advance them. In addition, our cell therapy assets are pre-clinical. Even if adequate funding and partnership opportunities are available, there is no guarantee that we will be successful in advancing one or more product candidates into and through clinical development. In addition, most of the efforts being made on behalf of AgenTus Therapeutics are being led by a separate AgenTus chief executive officer, utilizing Agenus' management team and internal G&A resources. The current structure could distract management and divert Agenus resources from Agenus' own core pipeline and programs.

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The cell therapy assets necessary to enable AgenTus Therapeutics are currently owned or controlled by Agenus in the United States and Switzerland. In connection with capitalizing AgenTus Therapeutics, these assets will be transferred or licensed to new legal entities within the United States and Europe and potentially others. Transferring these assets or licensing them on an exclusive basis would require that taxes be paid based on the fair market value of the assets. While we expect to have adequate net operating losses to offset any tax liabilities, there is no guarantee that this will be the case in all relevant jurisdictions. Moreover, we have previously disclosed our interest in potentially issuing a tax-free dividend to Agenus' stockholders in the form of stock of AgenTus Therapeutics. There is no guarantee that any such dividend will be tax-free or that it will be issued at all, or the timing thereof. If we issue a dividend in the form of stock, there could be adverse tax consequences for certain of our stockholders.

Calamities, power shortages or power interruptions could disrupt our business and materially adversely affect our operations.

If a natural disaster, power outage or other event occurred that prevented us from using all or a significant portion of our facilities, that damaged critical infrastructure (such as our manufacturing facility) or that otherwise disrupted operations, it may be difficult or, in certain cases, impossible for us to continue certain activities, such as for example our manufacturing capabilities, for a substantial period of time. We own an antibody pilot plant manufacturing facility and lease additional office space in Berkeley, CA. This location is in an area of seismic activity near active earthquake faults. Any earthquake, terrorist attack, fire, power shortage or other calamity affecting our facilities or those of third parties upon whom we depend may disrupt our business and could have a material adverse effect on our business, results of operations, financial condition and prospects. The disaster recovery and business continuity plans we have in place currently are limited and are unlikely to prove adequate in the event of a serious disaster or similar event. We may incur substantial expenses and delays as a result of the limited nature of our disaster recovery and business continuity plans, which could have a material adverse effect on our business.

We are dependent upon our collaboration with Gilead to further develop and commercialize certain of our antibody programs. If we or Gilead fail to perform as expected, the potential for us to generate future revenues under the collaboration could be significantly reduced, the development and/or commercialization of these antibodies may be terminated or substantially delayed, and our business could be adversely affected.

In December 2018, we entered into a series of agreements with Gilead to collaborate on the development and commercialization of up to five novel I-O therapies. Pursuant to the collaboration agreements, Gilead received (i) worldwide exclusive rights to AGEN1423, a bispecific antibody, (ii) the exclusive option to license exclusively AGEN1223, a bispecific antibody, and AGEN2373, a monospecific antibody, and (iii) the right of first negotiation for two additional, undisclosed programs. Gilead has the exclusive right to develop and commercialize AGEN1423, and we are eligible to receive potential development and commercial milestones of up to \$552.5 million in the aggregate, as well as tiered royalty payments on aggregate net sales ranging from the high single digit to mid-teen percent, subject to certain reductions under certain circumstances. Accordingly, the timely and successful completion by Gilead of clinical development and commercialization activities will significantly affect the timing and amount of any milestones or royalties we may receive for this program. Gilead's activities will be influenced by, among other things, the efforts and allocation of resources by Gilead, which we cannot control. With respect to the option programs, we are responsible for developing each program up to the option decision point, at which time Gilead may acquire exclusive rights to each program on option exercise. During the option period, we are eligible to receive milestones of up to \$30.0 million in the aggregate. If Gilead exercises an option, it would be required to pay an upfront license exercise fee of \$50.0 million for each option that is exercised. Following any option exercise, we would be eligible to receive additional development and commercial milestones of up to \$520.0 million in the aggregate for each such option program, as well as tiered royalty payments on aggregate net sales ranging from the high single digit to mid-teen percent, subject to certain reductions under certain circumstances. For either, but not both, of the option programs, we will have the right to opt-in to share Gilead's development and commercialization costs in the United State for such option program in exchange for a profit (loss) share on a 50:50 basis and revised milestone payments. There is no guarantee that we will receive any fees, milestones or royalties from Gilead. If Gilead does not exercise its

option for either of the option programs, there is no guarantee that we will be able to advance any such program ourselves or with another partner. If we wanted to partner either of the programs that are subject to a right of first negotiation with a third party other than Gilead, such discussions could be delayed and ultimately terminated as a result of Gilead's right of first negotiation. Accordingly, we may not be able to partner either of these programs with a third party other than Gilead on attractive terms, if at all.

We are dependent upon our collaboration with Incyte to further develop, manufacture and commercialize antibodies against certain targets. If we or Incyte fail to perform as expected, the potential for us to generate future revenues under the collaboration could be significantly reduced, the development and/or commercialization of these antibodies may be terminated or substantially delayed, and our business could be adversely affected.

In February 2017, we amended the terms of our collaboration agreement with Incyte to, among other things, convert the GITR and OX40 programs from profit-share programs, where we and Incyte shared all costs and profits on a 50:50 basis, to royalty-bearing

programs, where Incyte funds 100% of the costs and we are eligible for potential milestones and royalties. In addition, the profit-share programs relating to TIGIT and one undisclosed target were removed from the collaboration, with TIGIT reverting to Agenus and the undisclosed target reverting to Incyte, each with a potential 15% royalty to the other party on any global net sales. The remaining three royalty-bearing programs in the collaboration targeting TIM-3, LAG-3 and one undisclosed target remain unchanged, and there are no more profit-share programs under the collaboration. For each program in the collaboration, we serve as the lead for pre-clinical development activities through the filing of an IND, and Incyte has exclusive rights and all decision-making authority for manufacturing, clinical development and commercialization. Accordingly, the timely and successful completion by Incyte of clinical development and commercialization activities will significantly affect the timing and amount of any royalties or milestones we may receive under the collaboration agreement. In addition, in March 2017 we transferred manufacturing responsibilities to Incyte for antibodies under that collaboration. Any delays or weaknesses in the ability of Incyte to successfully manufacture could have an adverse impact on those programs. Incyte's activities will be influenced by, among other things, the efforts and allocation of resources by Incyte, which we cannot control. If Incyte does not perform in the manner we expect or fulfill its responsibilities in a timely manner, or at all, the clinical development, manufacturing, regulatory approval, and commercialization efforts related to antibodies under the collaboration could be delayed or terminated. There can be no assurance that any of the development, regulatory or sales milestones will be achieved, or that we will receive any future milestone or royalty payments under the collaboration agreement. In September 2018, we sold to XOMA (US) LLC a portion of the royalties and milestones we are entitled to receive from Incyte.

In addition, our collaboration with Incyte may be unsuccessful due to other factors, including, without limitation, the following:

- Incyte may terminate the agreement or any individual program for convenience upon 12 months' notice;
- Incyte has control over the development of assets in the collaboration;
- Incyte may change the focus of its development and commercialization efforts or prioritize other programs more highly and, accordingly, reduce the efforts and resources allocated to our collaboration;
- Incyte may choose not to develop and commercialize antibody products, if any, in all relevant markets or for one or more indications, if at all; and
- If Incyte is acquired during the term of our collaboration, the acquirer may have competing programs or different strategic priorities that could cause it to reduce its commitment to our collaboration.

If Incyte terminates our collaboration agreement, we may need to raise additional capital and may need to identify and come to agreement with another collaboration partner to advance certain of our antibody programs. Even if we are able to find another partner, this effort could cause delays in our timelines and/or additional expenses, which could adversely affect our business prospects and the future of our antibody product candidates under the collaboration.

Comprehensive tax reform legislation could adversely affect our business and financial condition.

On December 22, 2017, President Trump signed into law the "Tax Cuts and Jobs Act" (the "TCJA") that significantly reformed the Internal Revenue Code of 1986, as amended. The TCJA, among other things, includes changes to U.S. federal tax rates, imposes significant additional limitations on the deductibility of interest and net operating loss carryforwards, allows for the expensing of capital expenditures, and puts into effect the migration from a "worldwide" system of taxation to a territorial system. Our net deferred tax assets and liabilities were revalued at the newly enacted U.S. corporate rate. We did not recognize any tax expense in the year of enactment as our net deferred tax assets have a full valuation allowance recorded. We continue to examine the impact this tax reform legislation may have on our business. The impact of this tax reform is uncertain and could be adverse.

#### Risks Related to Regulation of the Biopharmaceutical Industry

The drug development and approval process is uncertain, time-consuming, and expensive.

Drug development, including non-clinical testing and clinical development, and the process of obtaining regulatory approvals for new therapeutic products, is lengthy, expensive, and uncertain. For example, as of December 31, 2018, we had spent more than 20 years and \$809.2 million on our research and development programs. The development and regulatory approval processes also can vary substantially based on the therapeutic area, type, complexity, and novelty of the product. We must provide regulatory authorities with manufacturing, product characterization, and pre-clinical and clinical data demonstrating that our product candidates are safe and effective before they can be approved for commercial sale. It may take us many years to complete our testing, and failure can occur at any stage. Results of pre-clinical studies do not necessarily predict clinical results, and promising results in early clinical studies might not be confirmed in later studies. Any pre-clinical or clinical test may fail to produce results satisfactory to regulatory authorities for many reasons, including but not limited to emerging manufacturing or control issues, limitations of pre-clinical assessments, difficulties to enroll a sufficient number of patients, changing therapeutic landscape or failure to prospectively identify the benefit/risk profile of the new product. Pre-clinical and clinical data can be interpreted in different ways, which could delay, limit, or prevent



regulatory approval. Negative or inconclusive results from a pre-clinical study or clinical trial, adverse medical events during a clinical trial, or safety issues emerging with products of the same class of drug could require additional studies or cause a program to be terminated, even if other studies or trials relating to the program are successful. We or the FDA, other regulatory agencies, or an institutional review board may suspend or terminate human clinical trials at any time on various grounds.

The timing and success of a clinical trial is dependent on obtaining and maintaining sufficient cash resources, successful production of clinical trial material, enrolling sufficient patients in a timely manner, avoiding or mitigating serious or significant adverse patient reactions, and demonstrating efficacy of the product candidate in order to support a favorable risk versus benefit profile, among other considerations. The timing and success of our clinical trials, in particular, are also dependent on clinical sites and regulatory authorities accepting each trial's protocol, statistical analysis plan, product characterization tests, and final clinical results. In addition, regulatory authorities may request additional information or data that is not readily available. Delays in our ability to respond to such requests would delay, and failure to adequately address concerns would prevent, our commercialization efforts. We have encountered in the past, and may encounter in the future, delays in initiating trial sites and enrolling patients into our clinical trials. Future enrollment delays will postpone the dates by which we expect to complete the impacted trials and the potential receipt of regulatory approval. There is no guarantee we will successfully initiate and/or complete our clinical trials.

Delays or difficulties in obtaining regulatory approvals or clearances for our product candidates may:

- adversely affect the marketing of any products we or our licensees or collaborators develop;
- impose significant additional costs on us or our licensees or collaborators;
- diminish any competitive advantages that we or our licensees or collaborators may attain;
- limit our ability to receive royalties and generate revenue and profits; and
- adversely affect our business prospects and ability to obtain financing.

Delays or failures in our receiving regulatory approval for our product candidates in a timely manner may result in us having to incur additional development expense and subject us to having to secure additional financing. As a result, we may not be able to commercialize them in the time frame anticipated, and our business will suffer.

Even if we or our partners receive marketing approval for our product candidates, such product approvals could be subject to restrictions or withdrawals. Regulatory requirements are subject to change. Further, even if we or our partners receive marketing approval, we may not receive sufficient coverage and adequate reimbursement for our products.

Regulatory authorities generally approve products for particular indications. If an approval is for a limited indication, this limitation reduces the size of the potential market for that product. Product approvals, once granted, are subject to continual review and periodic inspections by regulatory authorities. Our operations and practices are subject to regulation and scrutiny by the United States government, as well as governments of any other countries in which we do business or conduct activities. Later discovery of previously unknown problems or safety issues, and/or failure to comply with domestic or foreign laws, knowingly or unknowingly, can result in various adverse consequences, including, among other things, possible delay in approval or refusal to approve a product, warning letters, fines, injunctions, civil penalties, recalls or seizures of products, total or partial suspension of production, refusal of the government to renew marketing applications, complete withdrawal of a marketing application, corrective action requirements, and/or criminal prosecution, withdrawal of an approved product from the market, and/or exclusion from government health care programs. Such regulatory enforcement could have a direct and negative impact on the product for which approval is granted and could have a negative impact on the approval of any pending applications for marketing approval of new drugs or supplements to approved applications.

Because we operate in a highly regulated industry, regulatory authorities could take enforcement action against us in connection with our licensees' or collaborators', and/or our business and marketing activities for various reasons. For example, the Foreign Corrupt Practices Act prohibits U.S. companies and their representatives from offering,

promising, authorizing, or making payments to foreign governmental officials for the purpose of obtaining or retaining business abroad.

From time to time, new legislation is passed into law that could significantly change the statutory provisions governing the approval, manufacturing, and marketing of products regulated by the FDA and other foreign health authorities. Additionally, regulations and guidance are often revised or reinterpreted by health agencies in ways that may significantly affect our business and our products. It is impossible to predict whether further legislative changes will be enacted, or whether regulations, guidance, or interpretations will change, and what the impact of such changes, if any, may be. For example, the Patient Protection and Affordable Care Act and the Health Care and Education Affordability Reconciliation Act of 2010 (collectively the “ACA”), enacted in March 2010, substantially changed the way healthcare is financed by both governmental and private insurers, and significantly impacted the pharmaceutical industry. With regard to pharmaceutical products, among other things, ACA is expected to expand, increase, and change the methodology regarding industry rebates for drugs covered under Medicaid programs; impose an annual, nondeductible fee on any entity that manufactures or imports specific branded prescription drugs and biologic agents, apportioned among those entities

according to market share in certain government healthcare programs; expand eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to certain individuals with income at or below 133% of the federal poverty level; expand the entities eligible for discounts under the Public Health Service pharmaceutical pricing program; create a new Patient Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research; and make changes to the coverage requirements under the Medicare D program. Significant legislative changes to the ACA also appear possible in the 115<sup>th</sup> U.S. Congress under the Trump Administration.

We expect both government and private health plans to continue to require healthcare providers, including healthcare providers that may one day purchase our products, to contain costs and demonstrate the value of the therapies they provide. Even if our product candidates are approved, the commercial success of our products will depend substantially on the extent to which they are covered by third-party payors, including government health authorities and private health insurers. In the United States, no uniform policy of coverage and reimbursement for products exists among third-party payors, and coverage and reimbursement for products can differ significantly from payor to payor. If coverage and reimbursement are not available, or reimbursement is available only to limited levels, we or our collaborators may not be able to successfully commercialize our product candidates.

New data from our research and development activities, and/or resource considerations could modify our strategy and result in the need to adjust our projections of timelines and costs of programs.

Because we are focused on novel technologies, our research and development activities, including our nonclinical studies and clinical trials, involve the ongoing discovery of new facts and the generation of new data, based on which we determine next steps for a relevant program. These developments can occur with varying frequency and constitute the basis on which our business is conducted. We make determinations on an ongoing basis as to which of these facts or data will influence timelines and costs of programs. We may not always be able to make such judgments accurately, which may increase the costs we incur attempting to commercialize our product candidates. We monitor the likelihood of success of our initiatives and we may need to discontinue funding of such activities if they do not prove to be commercially feasible, due to our limited resources.

We may need to successfully address a number of technological challenges in order to complete development of our product candidates. Moreover, these product candidates may not be effective in treating any disease or may prove to have undesirable or unintended side effects, toxicities, or other characteristics that may preclude our obtaining regulatory approvals or prevent or limit commercial use.

#### Risks Related to Intellectual Property Rights

If we are unable to obtain and enforce patent protection for our product candidates and related technology, our business could be materially harmed.

We rely upon a combination of patents, trade secret protection and confidentiality agreements to protect the intellectual property related to our product candidates and technology. Any disclosure to or misappropriation by third parties of our confidential proprietary information could enable competitors to duplicate or surpass our technological achievements, eroding our competitive position in the market. Our patent applications may not result in issued patents, and, even if issued, the patents may be challenged and invalidated. Moreover, our patents and patent applications may not be sufficiently broad to prevent others from practicing our technologies or developing competing products. We also face the risk that others may independently develop similar or alternative technologies or may design around our proprietary property.

Issued patents may be challenged, narrowed, invalidated or circumvented. In addition, court decisions may introduce uncertainty in the enforceability or scope of patents owned by biotechnology companies. The legal systems of certain countries do not favor the aggressive enforcement of patents, and the laws of foreign countries may not allow us to

protect our inventions with patents to the same extent as the laws of the United States. Because patent applications in the United States and many foreign jurisdictions are typically not published until 18 months after filing, or in some cases not at all, and because publications of discoveries in scientific literature lag behind actual discoveries, we cannot be certain that we were the first to make the inventions claimed in our issued patents or pending patent applications, or that we were the first to file for protection of the inventions set forth in our patents or patent applications. As a result, we may not be able to obtain or maintain protection for certain inventions. Therefore, the enforceability and scope of our patents in the United States and in foreign countries cannot be predicted with certainty and, as a result, any patents that we own, or license may not provide sufficient protection against competitors. We may not be able to obtain or maintain patent protection from our pending patent applications, from those we may file in the future, or from those we may license from third parties. Moreover, even if we are able to obtain patent protection, such patent protection may be of insufficient scope to achieve our business objectives.

Patent terms may be inadequate to protect our competitive position on our product candidates for an adequate amount of time. Patents have a limited lifespan. In the United States, the natural expiration of a patent is generally 20 years after its effective filing date. Various extensions may be available; however, the life of a patent, and the protection it affords, is limited. Without patent protection for our product candidates, we may be open to competition from biosimilar or generic versions of our product candidates. Furthermore, the product development timeline for biotechnology products is lengthy and it is possible that our issued patents covering our product candidates in the United States and other jurisdictions may expire prior to commercial launch. For example, if we encounter delays in our development efforts, including our clinical trials, the period of time during which we could market our product candidates under patent protection could be reduced.

Our strategy depends on our ability to identify and seek patent protection for our discoveries. This process is expensive and time consuming, and we and our current or future licensors or licensees may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner or in all jurisdictions where protection may be commercially advantageous. It is also possible that we or our current licensors or licensees, or any future licensors or licensees, may not identify patentable aspects of inventions made in the course of development and commercialization activities in time to obtain patent protection on them. Therefore, these and any of our patents and applications may not be prosecuted and enforced in a manner consistent with the best interests of our business. Defects of form in the preparation or filing of our patents or patent applications may exist, or may arise in the future, for example with respect to proper priority claims, inventorship, etc. If we or our current licensors or licensees, or any future licensors or licensees, fail to establish, maintain or protect such patents and other intellectual property rights, such rights may be reduced or eliminated. If our current licensors or licensees, or any future licensors or licensees, are not fully cooperative or disagree with us as to the prosecution, maintenance or enforcement of any patent rights, such patent rights could be compromised. If there are material defects in the form or preparation of our patents or patent applications, such patents or applications may be invalid and unenforceable. Despite our efforts to protect our proprietary rights, unauthorized parties may be able to obtain and use information that we regard as proprietary. The issuance of a patent does not ensure that it is valid or enforceable, so even if we obtain patents, they may not be valid or enforceable against third parties. In addition, the issuance of a patent does not give us the right to practice the patented invention. Third parties may have blocking patents that could prevent us from marketing our own patented product and practicing our own patented technology. Any of these outcomes could impair our ability to prevent competition from third parties, which may have an adverse impact on our business.

The patent landscapes in the fields of antibody, vaccine, adjuvant and adoptive cell therapy development, manufacture and commercialization are crowded. For example, we are aware of third party patents directed to methods for identifying and producing therapeutic products such as antibodies, vaccines, adjuvants and adoptive cell therapies. We are also aware of third party patents directed to products targeting numerous antigens for which we also seek to identify, develop, and commercialize products. For example, some patents claim products based on competitive binding with existing products, some claim products based on specifying sequence or other structural information, and some claim various methods of discovery, production, or use of such products.

These or other third-party patents could impact our freedom to operate in relation to our technology platforms, as well as in relation to development and commercialization of products identified by us as therapeutic candidates. As we discover and develop our candidates, we will continue to conduct analyses of these third-party patents to determine whether we believe we might infringe them, and if so, whether they would be likely to be deemed valid and enforceable if challenged. If we determine that a license for a given patent or family of patents is necessary or desirable, there can be no guarantee that a license would be available on favorable terms, or at all. Inability to obtain a license on favorable terms, should such a license be determined to be necessary or desirable, could, without limitation, result in increased costs to design around the third-party patents, delay product launch, or result in cancellation of the affected program or cessation of use of the affected technology.

Third parties may also seek to market biosimilar versions of any approved products. Alternatively, third parties may seek approval to market their own products similar to or otherwise competitive with our products. In these

circumstances, we may need to defend and/or assert our patents, including by filing lawsuits alleging patent infringement. In any of these types of proceedings, a court or agency with jurisdiction may find our patents invalid and/or unenforceable. Even if we have valid and enforceable patents, these patents still may not provide protection against competing products or processes sufficient to achieve our business objectives.

We own, co-own or have exclusive rights to approximately 25 issued United States patents and approximately 75 issued foreign patents. We also own, co-own or have exclusive rights to approximately 35 pending United States patent applications and approximately 180 pending foreign patent applications. However, our patents may not protect us against our competitors. Our patent positions, and those of other biopharmaceutical, pharmaceutical and biotechnology companies, are generally uncertain and involve complex legal, scientific, and factual questions. The standards which the United States Patent and Trademark Office (“USPTO”) uses to grant patents, and the standards which courts use to interpret patents, are not always applied predictably or uniformly and can change, particularly as new technologies develop. Consequently, the level of protection, if any, that will be provided by our patents if we attempt to enforce them and they are challenged, is uncertain. In addition, the type and extent of patent claims that will be issued to us in the future is uncertain. Any patents that are issued may not contain claims that permit us to stop competitors from using similar technology.

Through our acquisitions of 4-AB, PhosImmune and certain assets of Celexion, we own, co-own, or have exclusive rights to a number of patents and patent applications directed to various methods and compositions, including methods for identifying therapeutic antibodies and product candidates arising out of such entities' technology platforms. In particular, we own patents and patent applications relating to our Retrocyte Display™ technology platform, a high throughput antibody expression platform for the identification of fully-human and humanized monoclonal antibodies. This patent family is projected to expire between 2029 and 2031. Through our acquisition of PhosImmune, we own, co-own, or have exclusive rights to patents and patent applications directed to various methods and compositions, including a patent directed to methods for identifying phosphorylated proteins using mass spectrometry. This patent is projected to expire in 2023. We also own patents and patent applications relating to the SECANT® platform, a platform used for the generation of novel monoclonal antibodies. This patent family is projected to expire between 2028 and 2029. In addition, as we advance our research and development efforts with our institutional and corporate collaborators, we are seeking patent protection for newly identified therapeutic antibodies and product candidates. We can provide no assurance that any of our patents, including the patents that we acquired or in-licensed in connection with our acquisitions of 4-AB, PhosImmune and certain assets of Celexion, will have commercial value, or that any of our existing or future patent applications, including the patent applications that we acquired or in-licensed in connection with our acquisitions of 4-AB, PhosImmune and certain assets of Celexion, will result in the issuance of valid and enforceable patents.

Our issued patents covering Prophage vaccine and methods of use thereof, alone or in combination with other agents, expired or will expire at various dates between 2015 and 2024. In particular, our issued U.S. patents covering Prophage composition of matter expired in 2015. In addition, our issued patents covering QS-21 Stimulon composition of matter expired in 2008. We continue to explore means of extending the life cycle of our patent portfolio.

The patent position of biopharmaceutical, pharmaceutical or biotechnology companies, including ours, is generally uncertain and involves complex legal and factual considerations. The standards which the USPTO and its foreign counterparts use to grant patents are not always applied predictably or uniformly and can change. There is also no uniform, worldwide policy regarding the subject matter and scope of claims granted or allowable in biopharmaceutical, pharmaceutical or biotechnology patents. The laws of some foreign countries do not protect proprietary information to the same extent as the laws of the United States, and many companies have encountered significant problems and costs in protecting their proprietary information in these foreign countries. Outside the United States, patent protection must be sought in individual jurisdictions, further adding to the cost and uncertainty of obtaining adequate patent protection outside of the United States. Accordingly, we cannot predict whether additional patents protecting our technology will issue in the United States or in foreign jurisdictions, or whether any patents that do issue will have claims of adequate scope to provide competitive advantage. Moreover, we cannot predict whether third parties will be able to successfully obtain claims or the breadth of such claims. The allowance of broader claims may increase the incidence and cost of patent interference proceedings, opposition proceedings, post-grant review, inter partes review, and/or reexamination proceedings, the risk of infringement litigation, and the vulnerability of the claims to challenge. On the other hand, the allowance of narrower claims does not eliminate the potential for adversarial proceedings and may fail to provide a competitive advantage. Our issued patents may not contain claims sufficiently broad to protect us against third parties with similar technologies or products or provide us with any competitive advantage.

We may become involved in lawsuits to protect or enforce our patents, which could be expensive, time consuming and unsuccessful.

Third parties may infringe or misappropriate our intellectual property, including our existing patents, patents that may issue to us in the future, or the patents of our licensors or licensees to which we have a license. As a result, we may be required to file infringement claims to stop third-party infringement or unauthorized use. Further, we may not be able to prevent, alone or with our licensors or licensees, misappropriation of our intellectual property rights, particularly in countries where the laws may not protect those rights as fully as in the United States.

If we or one of our licensors or licensees were to initiate legal proceedings against a third party to enforce a patent covering our product candidates, the defendant could counterclaim that the patent covering our product candidates is invalid and/or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity and/or unenforceability are commonplace, and there are numerous grounds upon which a third party can assert invalidity or unenforceability of a patent.

In addition, within and outside of the United States, there has been a substantial amount of litigation and administrative proceedings, including interference and reexamination proceedings before the USPTO or oppositions and other comparable proceedings in various foreign jurisdictions, regarding patent and other intellectual property rights in the biopharmaceutical industry. Notably, the Leahy-Smith America Invents Act, or the American Invents Act (“AIA”), introduced new procedures, including inter partes review and post grant review. These procedures may be used by competitors to challenge the scope and/or validity of our patents, including those patents perceived by our competitors as blocking entry into the market for their products, and the outcome of such challenges.



Even after they have been issued, our patents and any patents which we license may be challenged, narrowed, invalidated or circumvented. If our patents are invalidated or otherwise limited or will expire prior to the commercialization of our product candidates, other companies may be better able to develop products that compete with ours, which could adversely affect our competitive business position, business prospects and financial condition.

The following are non-exclusive examples of litigation and other adversarial proceedings or disputes that we could become a party to involving our patents or patents licensed to us:

- we or our collaborators may initiate litigation or other proceedings against third parties to enforce our patent rights;
- third parties may initiate litigation or other proceedings seeking to invalidate patents owned by or licensed to us or to obtain a declaratory judgment that their product or technology does not infringe our patents or patents licensed to us;
- third parties may initiate opposition proceedings, post-grant review, inter partes review, or reexamination proceedings challenging the validity or scope of our patent rights, requiring us or our collaborators and/or licensors or licensees to participate in such proceedings to defend the validity and scope of our patents;
- there may be a challenge or dispute regarding inventorship or ownership of patents currently identified as being owned by or licensed to us;
- the USPTO may initiate an interference or derivation proceeding between patents or patent applications owned by or licensed to us and those of our competitors, requiring us or our collaborators and/or licensors or licensees to participate in an interference or derivation proceeding to determine the priority of invention, which could jeopardize our patent rights; or
- third parties may seek approval to market biosimilar versions of our future approved products prior to expiration of relevant patents owned by or licensed to us, requiring us to defend our patents, including by filing lawsuits alleging patent infringement.

These lawsuits and proceedings would be costly and could affect our results of operations and divert the attention of our managerial and scientific personnel. There is a risk that a court or administrative body could decide that our patents are invalid or not infringed by a third party's activities, or that the scope of certain issued claims must be further limited. An adverse outcome in a litigation or proceeding involving our own patents could limit our ability to assert our patents against these or other competitors, affect our ability to receive royalties or other licensing consideration from our licensees, and may curtail or preclude our ability to exclude third parties from making, using and selling similar or competitive products. An adverse outcome may also put our pending patent applications at risk of not issuing, or issuing with limited and potentially inadequate scope to cover our product candidates. The outcome following legal assertions of invalidity and unenforceability is unpredictable. With respect to the validity question, for example, we cannot be certain that there is no invalidating prior art, of which we and the patent examiner were unaware during prosecution. Additionally, it is also possible that prior art of which we are aware, but which we do not believe affects the validity or enforceability of a claim, may, nonetheless, ultimately be found by a court of law or an administrative panel to affect the validity or enforceability of a claim, for example, if a priority claim is found to be improper. If a defendant were to prevail on a legal assertion of invalidity and/or unenforceability, we could lose at least part, and perhaps all, of the patent protection on our relevant product candidates. Such a loss of patent protection could have a material adverse impact on our business.

Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation or administrative proceedings, there is a risk that some of our confidential information could be compromised by disclosure. In addition, during the course of litigation or administrative proceedings, there could be public announcements of the results of hearings, motions or other interim proceedings or developments or public access to related documents. If investors perceive these results to be negative, the market price for our common stock could be significantly harmed. Any of these occurrences could adversely affect our competitive business position, business prospects, and financial condition.

Intellectual property rights do not necessarily address all potential threats to our competitive advantage. The degree of future protection for our proprietary rights is uncertain because legal means afford only limited protection and may not adequately protect our rights or permit us to gain or keep our competitive advantage. For example:

- others may be able to develop a platform that is similar to, or better than, ours in a way that is not covered by the claims of our patents;
- others may be able to make compounds that are similar to our product candidates but that are not covered by the claims of our patents;
- we might not have been the first to make the inventions covered by patents or pending patent applications;
- we might not have been the first to file patent applications for these inventions;

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- any patents that we obtain may not provide us with any competitive advantages or may ultimately be found invalid or unenforceable; or
- we may not develop additional proprietary technologies that are patentable.

Our commercial success depends significantly on our ability to operate without infringing the patents and other proprietary rights of third parties.

Our success will depend in part on our ability to operate without infringing the proprietary rights of third parties. Other entities may have or obtain patents or proprietary rights that could limit our ability to make, use, sell, offer for sale or import our future approved products or impair our competitive position. In particular, the patent landscapes around the discovery, development, manufacture and commercial use of our product candidates are crowded.

Third parties may have or obtain valid and enforceable patents or proprietary rights that could block us from developing product candidates using our technology. Our failure to obtain a license to any technology that we require may materially harm our business, financial condition and results of operations. Moreover, our failure to maintain a license to any technology that we require may also materially harm our business, financial condition, and results of operations. Furthermore, we would be exposed to a threat of litigation.

In the biopharmaceutical industry, significant litigation and other proceedings regarding patents, patent applications, trademarks and other intellectual property rights have become commonplace. The types of situations in which we may become a party to such litigation or proceedings include:

- we or our collaborators may initiate litigation or other proceedings against third parties seeking to invalidate the patents held by those third parties or to obtain a judgment that our products or processes do not infringe those third parties' patents;
- if our competitors file patent applications that claim technology also claimed by us or our licensors or licensees, we or our licensors or licensees may be required to participate in interference, derivation or other proceedings to determine the priority of invention, which could jeopardize our patent rights and potentially provide a third party with a dominant patent position;
- if third parties initiate litigation claiming that our processes or products infringe their patent or other intellectual property rights, we and our collaborators will need to defend against such proceedings; and
- if a license to necessary technology is terminated, the licensor may initiate litigation claiming that our processes or products infringe or misappropriate their patent or other intellectual property rights and/or that we breached our obligations under the license agreement, and we and our collaborators would need to defend against such proceedings.

These lawsuits would be costly and could affect our results of operations and divert the attention of our management and scientific personnel. There is a risk that a court would decide that we or our collaborators are infringing the third party's patents and would order us or our collaborators to stop the activities covered by the patents. In that event, we or our collaborators may not have a viable alternative to the technology protected by the patent and may need to halt work on the affected product candidate or cease commercialization of an approved product. In addition, there is a risk that a court will order us or our collaborators to pay the other party damages. An adverse outcome in any litigation or other proceeding could subject us to significant liabilities to third parties and require us to cease using the technology that is at issue or to license the technology from third parties. We may not be able to obtain any required licenses on commercially acceptable terms or at all. Any of these outcomes could have a material adverse effect on our business.

The biopharmaceutical industry has produced a significant number of patents, and it may not always be clear to industry participants, including us, which patents cover various types of products or methods of use. The coverage of patents is subject to interpretation by the courts, and the interpretation is not always uniform or predictable. If we are sued for patent infringement, we would need to demonstrate that our products or methods either do not infringe the patent claims of the relevant patent or that the patent claims are invalid, and we may not be able to do this. Proving invalidity is difficult. For example, in the United States, proving invalidity requires a showing of clear and convincing evidence to overcome the presumption of validity enjoyed by issued patents. Even if we are successful in these

proceedings, we may incur substantial costs and divert management's time and attention in pursuing these proceedings, which could have a material adverse effect on us. If we are unable to avoid infringing the patent rights of others, we may be required to seek a license, defend an infringement action or challenge the validity of the patents in court. Patent litigation is costly and time consuming. We may not have sufficient resources to bring these actions to a successful conclusion. In addition, if we do not obtain a license, develop or obtain non-infringing technology, fail to defend an infringement action successfully or have infringed patents declared invalid, we may incur substantial monetary damages, encounter significant delays in bringing our product candidates to market and be precluded from manufacturing or selling our product candidates.

The cost of any patent litigation or other proceeding, even if resolved in our favor, could be substantial. Some of our competitors may be able to sustain the cost of such litigation and proceedings more effectively than we can because of their substantially greater resources. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have a material adverse effect on our ability to compete in the marketplace. Patent litigation and other proceedings may also absorb significant management time.

If we fail to comply with our obligations under our intellectual property licenses with third parties, we could lose license rights that are important to our business.

We are currently party to various intellectual property license agreements. These license agreements impose, and we expect that future license agreements may impose, various diligence, milestone payment, royalty, insurance and other obligations on us. These licenses typically include an obligation to pay an upfront payment, yearly maintenance payments and royalties on sales. If we fail to comply with our obligations under the licenses, the licensors may have the right to terminate their respective license agreements, in which event we might not be able to market any product that is covered by the agreements. Termination of the license agreements or reduction or elimination of our licensed rights may result in our having to negotiate new or reinstated licenses with less favorable terms, which could adversely affect our competitive business position and harm our business.

If we are unable to protect the confidentiality of our proprietary information, the value of our technology and products could be adversely affected.

In addition to patent protection, we also rely on other proprietary rights, including protection of trade secrets, and other proprietary information. To maintain the confidentiality of trade secrets and proprietary information, we enter into confidentiality agreements with our employees, consultants, collaborators and others upon the commencement of their relationships with us. These agreements require that all confidential information developed by the individual or made known to the individual by us during the course of the individual's relationship with us be kept confidential and not disclosed to third parties. Our agreements with employees and our personnel policies also provide that any inventions conceived by the individual in the course of rendering services to us shall be our exclusive property. However, we may not obtain these agreements in all circumstances, and individuals with whom we have these agreements may not comply with their terms. Thus, despite such agreement, such inventions may become assigned to third parties. In the event of unauthorized use or disclosure of our trade secrets or proprietary information, these agreements, even if obtained, may not provide meaningful protection, particularly for our trade secrets or other confidential information. To the extent that our employees, consultants or contractors use technology or know-how owned by third parties in their work for us, disputes may arise between us and those third parties as to the rights in related inventions. To the extent that an individual who is not obligated to assign rights in intellectual property to us is rightfully an inventor of intellectual property, we may need to obtain an assignment or a license to that intellectual property from that individual, or a third party or from that individual's assignee. Such assignment or license may not be available on commercially reasonable terms or at all.

Adequate remedies may not exist in the event of unauthorized use or disclosure of our proprietary information. The disclosure of our trade secrets would impair our competitive position and may materially harm our business, financial condition and results of operations. Costly and time-consuming litigation could be necessary to enforce and determine the scope of our proprietary rights, and failure to maintain trade secret protection could adversely affect our competitive business position. In addition, others may independently discover or develop our trade secrets and proprietary information, and the existence of our own trade secrets affords no protection against such independent discovery.

As is common in the biopharmaceutical industry, we employ individuals who were previously or concurrently employed at research institutions and/or other biopharmaceutical, biotechnology or pharmaceutical companies, including our competitors or potential competitors. We may be subject to claims that these employees, or we, have inadvertently or otherwise used or disclosed trade secrets or other proprietary information of their former employers,

or that patents and applications we have filed to protect inventions of these employees, even those related to one or more of our product candidates, are rightfully owned by their former or concurrent employer. Litigation may be necessary to defend against these claims. Even if we are successful in defending against these claims, litigation could result in substantial costs and be a distraction to management.

Obtaining and maintaining our patent protection depends on compliance with various procedural, documentary, fee payment and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for non-compliance with these requirements.

Periodic maintenance fees, renewal fees, annuity fees and various other governmental fees on patents and/or applications will be due to the USPTO and various foreign patent offices at various points over the lifetime of our patents and/or applications. We have systems in place to remind us to pay these fees, and we rely on our outside counsel or service providers to pay these fees when due. Additionally, the USPTO and various foreign patent offices require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. We employ reputable law firms and other professionals to

help us comply, and in many cases, an inadvertent lapse can be cured by payment of a late fee or by other means in accordance with rules applicable to the particular jurisdiction. However, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. If such an event were to occur, it could have a material adverse effect on our business. In addition, we are responsible for the payment of patent fees for patent rights that we have licensed from other parties.

If any licensor of these patents does not itself elect to make these payments, and we fail to do so, we may be liable to the licensor for any costs and consequences of any resulting loss of patent rights.

Changes in U.S. patent law could diminish the value of patents in general, thereby impairing our ability to protect our product candidates.

Obtaining and enforcing patents in the biopharmaceutical industry involves both technological and legal complexity, and therefore, is costly, time-consuming and inherently uncertain. In addition, the United States has enacted and implemented wide-ranging patent reform legislation. Further, recent U.S. Supreme Court rulings have either narrowed the scope of patent protection available in certain circumstances or weakened the rights of patent owners in certain situations. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents, once obtained.

For our U.S. patent applications containing a claim not entitled to priority before March 16, 2013, there is a greater level of uncertainty in the patent law. In September 2011, AIA was signed into law. The AIA includes a number of significant changes to U.S. patent law, including provisions that affect the way patent applications are prosecuted and also affect patent litigation. The USPTO has developed regulations and procedures to govern administration of the AIA, and many of the substantive changes to patent law associated with the AIA. It is not clear what other, if any, impact the AIA will have on the operation of our business. Moreover, the AIA and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could have a material adverse effect on our business and financial condition.

An important change introduced by the AIA is that, as of March 16, 2013, the United States transitioned to a “first-inventor-to- file” system for deciding which party should be granted a patent when two or more patent applications are filed by different parties claiming the same invention. A third party that files a patent application in the USPTO after that date but before us could therefore be awarded a patent covering an invention of ours even if we had made the invention before it was made by the third party. This requires us to be cognizant going forward of the time from invention to filing of a patent application. Furthermore, our ability to obtain and maintain valid and enforceable patents depends on whether the differences between our technology and the prior art allow our technology to be patentable over the prior art. Since patent applications in the United States and most other countries are confidential for a period of time after filing, we cannot be certain that we were the first to either (i) file any patent application related to our product candidates or (ii) invent any of the inventions claimed in our patents or patent applications.

Among some of the other changes introduced by the AIA are changes that limit where a patentee may file a patent infringement suit and providing opportunities for third parties to challenge any issued patent in the USPTO. This applies to all of our U.S. patents, even those issued before March 16, 2013. Because of a lower evidentiary standard in USPTO proceedings compared to the evidentiary standard in United States federal court necessary to invalidate a patent claim, a third party could potentially provide evidence in a USPTO proceeding sufficient for the USPTO to hold a claim invalid even though the same evidence would be insufficient to invalidate the claim if first presented in a district court action. Accordingly, a third party may attempt to use the USPTO procedures to invalidate our patent claims that would not have been invalidated if first challenged by the third party as a defendant in a district court action.

We may be subject to claims that our employees, consultants or independent contractors have wrongfully used or disclosed confidential information of third parties.

We may have received confidential and proprietary information from third parties. In addition, we employ individuals who were previously employed at other biopharmaceutical, biotechnology or pharmaceutical companies. We may be subject to claims that we or our employees, consultants or independent contractors have inadvertently or otherwise improperly used or disclosed confidential information of these third parties or our employees' former employers. Further, we may be subject to ownership disputes in the future arising, for example, from conflicting obligations of consultants or others who are involved in developing our product candidates. We may also be subject to claims that former employees, consultants, independent contractors, collaborators or other third parties have an ownership interest in our patents or other intellectual property. Litigation may be necessary to defend against these and other claims challenging our right to and use of confidential and proprietary information. If we fail in defending any such claims, in addition to paying monetary damages, we may lose our rights therein. Such an outcome could have a material adverse effect on our business. Even if we are successful in defending against these claims, litigation could result in substantial cost and be a distraction to our management and employees.



We may not be able to protect our intellectual property rights throughout the world.

Filing, prosecuting and defending patents on our product candidates in all countries throughout the world would be prohibitively expensive. The requirements for patentability may differ in certain countries, particularly developing countries. For example, China has a heightened requirement for patentability, and specifically requires a detailed description of medical uses of a claimed drug. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as laws in the United States. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and, further, may export otherwise infringing products to territories where we have patent protection, but enforcement on infringing activities is inadequate. These products may compete with our product candidates, and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents and other intellectual property protection, particularly those relating to biopharmaceuticals, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our proprietary rights generally. Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly and our patent applications at risk of not issuing, and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded, if any, may not be commercially meaningful. In addition, certain countries in Europe and certain developing countries, including India and China, have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties. In those countries, we may have limited remedies if our patents are infringed or if we are compelled to grant a license to our patents to a third party, which could materially diminish the value of those patents. This could limit our potential revenue opportunities. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we own or license. Finally, our ability to protect and enforce our intellectual property rights may be adversely affected by unforeseen changes in foreign intellectual property laws.

#### Risks Related to Litigation

We may face litigation or regulatory investigations that could result in substantial damages and may divert management's time and attention from our business.

From time to time we may become a party to legal proceedings, claims and investigations that arise in the ordinary course of business such as, but not limited to, patent, employment, securities, commercial and environmental matters. While we currently believe that the ultimate outcome of any of these proceedings will not have a material adverse effect on our financial position, results of operations, or liquidity, litigation is subject to inherent uncertainty. Furthermore, litigation and regulatory investigations consume both cash and management attention.

We maintain property and general commercial insurance coverage as well as errors and omissions insurance policies. This insurance coverage may not be sufficient to cover us for all potential claims or a claim may be made for which we are not covered by insurance, in which case the damages could have a material and adverse effect on the business.

If we or our employees fail to comply with laws or regulations, it could adversely impact our reputation, business and stock price.

We are exposed to the risk of employee fraud or other misconduct. Misconduct by employees could include intentional and/or negligent failures to comply with FDA regulations, to provide accurate information to the FDA, to comply with manufacturing standards we have established, to comply with federal and state health care fraud and

abuse, transparency, and/or data privacy and security laws and regulations, to report financial information or data accurately or to disclose unauthorized activities to us. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, kickbacks, self-dealing and other abusive practices; to promote transparency; and to protect the privacy and security of patient data. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements.

While we have adopted a corporate compliance program, we may not be able to protect against all potential issues of noncompliance. Efforts to ensure that our business complies with all applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations, or case law involving applicable laws and regulations.

Employee misconduct could also involve the improper use or disclosure of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. In addition, during the course of our operations, our directors, executives and employees may have access to material, nonpublic information regarding our business, our results of operations or potential transactions we are considering. We may not be able to prevent a director, executive or employee from trading in our common stock on the basis of, or while having access to, material, nonpublic information. If a director, executive or employee was to be investigated, or an action was to be brought against a director, executive or employee for insider trading, it could have a negative impact on our reputation and our stock price. Such a claim, with or without merit, could also result in substantial expenditures of time and money, and divert the attention of our management team.

Product liability and other claims against us may reduce demand for our products and/or result in substantial damages.

We face an inherent risk of product liability exposure related to testing our product candidates in human clinical trials and manufacturing antibodies in our Berkeley, CA facility and may face even greater risks if we ever sell products commercially. An individual may bring a product liability claim against us if one of our product candidates causes, or merely appears to have caused, an injury. Product liability claims may result in:

- regulatory investigations;
- injury to our reputation;
- withdrawal of clinical trial volunteers;
- costs of related litigation;
- substantial monetary awards to plaintiffs; and
- decreased demand for any future products.

We manufacture the Prophage vaccines from a patient's cancer cells, and medical professionals must inject the vaccines into the same patient from which they were manufactured. A patient may sue us if a hospital, a shipping company, or we fail to receive the removed cancer tissue or deliver that patient's vaccine. We do not have any other insurance that covers loss of or damage to the Prophage vaccines or tumor material, and we do not know whether such insurance will be available to us at a reasonable price or at all. We have limited product liability coverage for use of our product candidates. Our product liability policy provides \$10.0 million aggregate coverage and \$10.0 million per occurrence coverage. This limited insurance coverage may be insufficient to fully cover us for future claims.

We are also subject to laws generally applicable to businesses, including but not limited to, federal, state and local wage and hour, employee classification, mandatory healthcare benefits, unlawful workplace discrimination and whistle-blowing. Any actual or alleged failure to comply with any regulation applicable to our business or any whistle-blowing claim, even if without merit, could result in costly litigation, regulatory action or otherwise harm our business, results of operations, financial condition, cash flow and future prospects.

If we do not comply with environmental laws and regulations, we may incur significant costs and potential disruption to our business.

We use or may use hazardous, infectious, and radioactive materials, and recombinant DNA in our operations, which have the potential of being harmful to human health and safety or the environment. We store these hazardous (flammable, corrosive, toxic), infectious, and radioactive materials, and various wastes resulting from their use, at our facilities pending use and ultimate disposal. We are subject to a variety of federal, state, and local laws and regulations governing use, generation, storage, handling, and disposal of these materials. We may incur significant costs complying with both current and future environmental health and safety laws and regulations. In particular, we are subject to regulation by the Occupational Safety and Health Administration, the Environmental Protection Agency, the Drug Enforcement Agency, the Department of Transportation, the Centers for Disease Control and Prevention, the National Institutes of Health, the International Air Transportation Association, and various state and local agencies. At any time, one or more of the aforementioned agencies could adopt regulations that may affect our operations. We are also subject to regulation under the Toxic Substances Control Act and the Resource Conservation Development

programs.

Although we believe that our current procedures and programs for handling, storage, and disposal of these materials comply with federal, state, and local laws and regulations, we cannot eliminate the risk of accidents involving contamination from these materials. Although we have a workers' compensation liability policy, we could be held liable for resulting damages in the event of an accident or accidental release, and such damages could be substantially in excess of any available insurance coverage and could substantially disrupt our business.

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## Risks Related to our Common Stock

Provisions in our organizational documents could prevent or frustrate attempts by stockholders to replace our current management.

Our certificate of incorporation and bylaws contain provisions that could make it more difficult for a third party to acquire us without the consent of our Board of Directors. Our certificate of incorporation provides for a staggered board and removal of directors only for cause. Accordingly, stockholders may elect only a minority of our Board at any annual meeting, which may have the effect of delaying or preventing changes in management. In addition, under our certificate of incorporation, our Board of Directors may issue additional shares of preferred stock and determine the terms of those shares of stock without any further action by our stockholders. Our issuance of additional preferred stock could make it more difficult for a third party to acquire a majority of our outstanding voting stock and thereby effect a change in the composition of our Board of Directors. Our certificate of incorporation also provides that our stockholders may not take action by written consent. Our bylaws require advance notice of stockholder proposals and director nominations and permit only our president or a majority of the Board of Directors to call a special stockholder meeting. These provisions may have the effect of preventing or hindering attempts by our stockholders to replace our current management. In addition, Delaware law prohibits a corporation from engaging in a business combination with any holder of 15% or more of its capital stock until the holder has held the stock for three years unless, among other possibilities, the board of directors approves the transaction. Our Board of Directors may use this provision to prevent changes in our management. Also, under applicable Delaware law, our Board of Directors may adopt additional anti-takeover measures in the future.

Our stock has historically had low trading volume, and its public trading price has been volatile.

During the period from our initial public offering on February 4, 2000 to December 31, 2018, and the year ended December 31, 2018, the closing price of our common stock has fluctuated between \$1.59 (or \$0.27 pre-reverse stock split) and \$315.78 (or \$52.63 pre-reverse stock split) per share and \$1.59 and \$6.04 per share, respectively. The average daily trading volume for the year ended December 31, 2018 was approximately 1,538,510 shares, while the average daily trading volume for the year ended December 31, 2017 was approximately 1,174,002. The market may experience significant price and volume fluctuations that are often unrelated to the operating performance of individual companies. In addition to general market volatility, many factors may have a significant adverse effect on the market price of our stock, including:

- continuing operating losses, which we expect over the next several years as we continue our development activities;
- announcements of decisions made by public officials or delays in any such announcements;
- results of our pre-clinical studies and clinical trials or delays in anticipated timing;
- delays in our regulatory filings or those of our partners;
- announcements of new collaboration agreements with strategic partners or developments by our existing collaboration partners;
- announcements of acquisitions;
- announcements of technological innovations, new commercial products, failures of products, or progress toward commercialization by our competitors or peers;
- failure to realize the anticipated benefits of acquisitions;
- developments concerning proprietary rights, including patent and litigation matters;
- publicity regarding actual or potential results with respect to product candidates under development;
  - quarterly fluctuations in our financial results, including our average monthly cash used in operating activities;
- variations in the level of expenses related to any of our product candidates or clinical development programs;
- additions or departures of key management or scientific personnel;
- conditions or trends in the biopharmaceutical, biotechnology and pharmaceutical industries generally;
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other events or factors, including those resulting from war, incidents of terrorism, natural disasters or responses to these events;

• changes in accounting principles;

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general economic and market conditions and other factors that may be unrelated to our operating performance or the operating performance of our competitors, including changes in market valuations of similar companies; and sales of common stock by us or our stockholders in the future, as well as the overall trading volume of our common stock.

In the past, securities class action litigation has often been brought against a company following a significant decline in the market price of its securities. This risk is especially relevant for us because many biopharmaceutical, biotechnology and pharmaceutical companies experience significant stock price volatility.

The trading market for our common stock will depend in part on the research and reports that securities or industry analysts publish about us or our business. If one or more of the analysts who covers us downgrades our stock, or publishes inaccurate or unfavorable research about our business, our stock price would likely decline. If one or more of these analysts ceases coverage of us or fails to publish reports on us regularly, demand for our stock could decrease, which could cause our stock price and trading volume to decline.

The sale of a significant number of shares could cause the market price of our stock to decline.

The sale by us or the resale by stockholders of a significant number of shares of our common stock could cause the market price of our common stock to decline. As of March 11, 2019, we had 134,205,374 shares of common stock outstanding. All of these shares are eligible for sale on Nasdaq, although certain of the shares are subject to sales volume and other limitations. We have filed registration statements to permit the sale of approximately 31,200,000 shares of common stock under our equity incentive plans, and to permit the sale of 1,500,000 shares of common stock under our 2015 Inducement Equity Plan. We have also filed registration statements to permit the sale of approximately 167,000 shares of common stock under our Employee Stock Purchase Plan, to permit the sale of 425,000 shares of common stock under our Directors' Deferred Compensation Plan, to permit the sale of approximately 31,100,319 shares of common stock pursuant to various private placement agreements and to permit the sale of up to 50,000,000 shares of our common stock pursuant to our At Market Issuance Sales Agreement. As of the date of filing, an aggregate of approximately 63,749,000 of these shares remained available for sale. In October 2018, we completed a private placement of 18,459 shares of Series C-1 convertible preferred stock, convertible into 18,459,000 shares of common stock. The resale of all 18,459,000 shares of common stock underlying the 18,459 shares of Series C-1 convertible preferred stock was registered with the SEC pursuant to a Registration Statement on Form S-3 filed with the SEC on November 8, 2018 and declared effective on December 10, 2018. As part of our collaboration with Gilead, we completed a private placement of 11,111,111 shares of common stock in January 2019, the resale of which must be registered with the SEC by December 2019. In connection with our acquisition of 4-AB in February 2014, we are obligated to make contingent milestone payments to the former shareholders of 4-AB, payable in cash or shares of our common stock at our option, as follows (i) \$10.0 million upon our market capitalization exceeding \$750.0 million for 30 consecutive trading days prior to the earliest of (a) February 12, 2024, (b) the sale of 4-AB or (c) the sale of Agenus and (ii) \$10.0 million upon our market capitalization exceeding \$1.0 billion for 30 consecutive trading days prior to the earliest of (a) February 12, 2024, (b) the sale of 4-AB or (c) the sale of Agenus. In connection with our acquisition of PhosImmune in December 2015, we issued 1,631,521 shares of our common stock to the shareholders of PhosImmune and other third parties having a fair market value of approximately \$7.4 million at closing. In addition, we may be obligated in the future to pay certain contingent milestones payments, payable at our election in cash or shares of our common stock of up to \$35.0 million in the aggregate. If we elect to pay any of these contingent milestones in shares, we are obligated to file registration statements covering any such shares. The market price of our common stock may decrease based on the expectation of such sales.

As of December 31, 2018, warrants to purchase approximately 2,900,000 shares of our common stock with a weighted average exercise price per share of \$4.52 were outstanding.

As of December 31, 2018, options to purchase 18,613,822 shares of our common stock with a weighted average exercise price per share of \$4.15 were outstanding. These options are subject to vesting that occurs over a period of up to four years following the date of grant. As of December 31, 2018, we had 10,083,270 vested options and 2,213,967

non-vested shares outstanding.

As of December 31, 2018, our outstanding shares of Series A-1 Convertible Preferred Stock were convertible into 333,333 shares of our common stock.

As of December 31, 2018, our outstanding shares of Series C-1 Convertible Preferred Stock were convertible into 18,459,000 shares of our common stock. In February 2019, holders of shares of Series C-1 Convertible Preferred Stock converted a portion of such shares into 3,000,000 shares of our common stock.

Any Biotech Electronic Security Tokens (the “Tokens”) we issue will be convertible into common stock in the event AGEN2034 is not approved for commercial sale by the FDA before December 31, 2021, which would dilute our shareholders. If the price per share of our common stock at the time of conversion, based on a trailing weighted average, is \$10 or less, a holder of Tokens

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would be permitted to convert 10 Tokens for 1 share of common stock. If the price per share is above \$10, a holder would be permitted to convert 10 Tokens into a fraction of share of common stock with a value of \$10. The Company will retain the right to pay cash upon conversion, rather than deliver shares.

We may issue additional common stock, preferred stock, restricted stock units, or securities convertible into or exchangeable for our common stock. Furthermore, substantially all shares of common stock for which our outstanding stock options or warrants are exercisable are, once they have been purchased, eligible for immediate sale in the public market. The issuance of additional common stock, preferred stock, restricted stock units, or securities convertible into or exchangeable for our common stock or the exercise of stock options or warrants would dilute existing investors and could adversely affect the price of our securities. In addition, such securities may have rights senior to the rights of securities held by existing investors.

We do not intend to pay cash dividends on our common stock and, consequently your ability to obtain a return on your investment will depend on appreciation in the price of our common stock.

We have never declared or paid any cash dividend on our common stock and do not intend to do so in the foreseeable future. We currently anticipate that we will retain future earnings for the development, operation and expansion of our business. Therefore, the success of an investment in shares of our common stock will depend upon any future appreciation in their value. There is no guarantee that shares of our common stock will appreciate in value or maintain their current value.

Failure to maintain effective internal controls in accordance with Section 404 of the Sarbanes-Oxley Act of 2002 and to comply with changing regulation of corporate governance and public disclosure could have a material adverse effect on our operating results and the price of our common stock.

The Sarbanes-Oxley Act of 2002 and rules adopted by the SEC and Nasdaq have resulted in significant costs to us. In particular, our efforts to comply with Section 404 of the Sarbanes-Oxley Act of 2002 and related regulations regarding the required assessment of our internal control over financial reporting, and our independent registered public accounting firm's audit of internal control over financial reporting, have required commitments of significant management time. We expect these commitments to continue.

Our internal control over financial reporting (as defined in Rules 13a-15 of the Exchange Act) is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of our consolidated financial statements for external purposes in accordance with U.S. GAAP. Because of its inherent limitations, internal control over financial reporting may not prevent or detect all deficiencies or weaknesses in our financial reporting. While our management has concluded that there were no material weaknesses in our internal control over financial reporting as of December 31, 2018, our procedures are subject to the risk that our controls may become inadequate because of changes in conditions or as a result of a deterioration in compliance with such procedures. No assurance is given that our procedures and processes for detecting weaknesses in our internal control over financial reporting will be effective.

Changing laws, regulations and standards relating to corporate governance and public disclosure, are creating uncertainty for companies. Laws, regulations and standards are subject to varying interpretations in some cases due to their lack of specificity, and as a result, their application in practice may evolve over time as new guidance is provided, which could result in continuing uncertainty regarding compliance matters and higher costs caused by ongoing revisions to disclosure and governance practices. If we fail to comply with these laws, regulations and standards, our reputation may be harmed, and we might be subject to sanctions or investigation by regulatory authorities, such as the SEC. Any such action could adversely affect our operating results and the market price of our common stock.

Risks Related to our Tokens

There is no assurance that we will sell a sufficient number of tokens, if any, to meet our business or financial goals.

In February 2019, we announced the launch of our Tokens, which we intend to issue in accordance with Regulation D of the Securities Act of 1933, as amended (the “Securities Act”) and pursuant to a private placement offering memorandum (the “Offering”). We announced an anticipated closing date in March 2019 and the possibility for us to raise up to a maximum of \$100 million in the Offering. As of the date of this filing, we have not closed on the sale of any Tokens. The Tokens are being offered by us on a “best efforts basis,” meaning that there is no assurance that any or all of the offered Tokens will be sold and we can elect in our discretion not to issue any Tokens for any reason. In addition, we may sell Tokens in multiple rounds, and there can be no assurance that even if we issue tokens in an initial round that we will initiate or complete one or more subsequent rounds.

We intend to use any proceeds of the Offering to fund continued commercial manufacturing, commercialization readiness and clinical development activities focused on combinations of AGEN2034 with other therapies and in indications beyond cervical cancer. If we are unable to raise adequate funds in the Offering, our ability to expand development opportunities for AGEN2034 may be limited. If the Offering does not result in substantial proceeds, it could have a material adverse effect on our ability to fund these objectives and carry out our related business plans. If we were unable to obtain adequate funding from other sources, we would be required to make decisions about which businesses and projects to fund, and we might be required to decrease or eliminate expenditures that we believe would have been advisable.

There is no assurance that purchasers of our Tokens will receive a return on their investment.

Pursuant to the terms of the Offering, each Token will entitle its holder (each, a “Tokenholder”) to receive certain payments following the first commercial sale in the U.S. of AGEN2034, if it receives applicable regulatory approvals. The Tokens are highly speculative and any return on an investment in the Tokens is contingent upon numerous circumstances, many of which (including legal and regulatory conditions) are beyond our control. There is no assurance that purchasers will realize any return on their investments or that their entire investments will not be lost.

If the Company is successful in commercializing AGEN2034, a significant portion of the net sales of such product in the U.S. will be paid to Tokenholders until the Tokenholders are paid the full amount to which they are entitled pursuant to their purchase agreement. As a result, the Company may not receive the full amount of net sales of such product for an extended period of time, if ever.

Following an initial holding period, we intend to transfer the Tokens from a book-entry ledger to the blockchain, which utilizes technologies that are unproven.

Following the holding period required by Rule 144 under the Securities Act for restricted securities, we intend to transfer the record ownership of Tokens from book-entry ledger maintained by a transfer agent to the blockchain. There can be no assurance that we will be able to make such transfer due technical or other limitations, and the ownership of the Tokens may continue to be recorded in a book-entry ledger indefinitely, which could adversely impact their adoption and liquidity.

In the event that the Tokens are transferred to the blockchain, Tokenholders will be relying upon technologies that are new and unproven. The Tokens and their underlying blockchain may not function as intended, or might not be capable of completion, implementation or adoption for many reasons, including technological defects or the inability to scale as contemplated. Any failures of the smart contract to operate as expected may result in unintended transactions that cannot be reversed, and Tokenholders may have more limited remedies than are available in the traditional securities markets. In addition, these technologies are quickly changing and adapting, so the Tokens and their underlying technology could also become outdated or obsolete, particularly if there is a lack of interest in ongoing technological support for the Tokens. Moreover, we have not yet selected which blockchain to utilize, and there could be increased security risk with one blockchain over another, as well as potential vulnerability of some blockchains to a “51% attack” that could result in tampering with the ledger information. There can be no assurance that the selected blockchain will perform as intended once the Tokens are transferred.

We have not identified all the persons that we will need to provide services and functions critical to the maintenance of the Tokens and no assurance can be given that we will be able to engage all necessary persons on acceptable terms, if at all.

We need to identify and recruit additional qualified personnel with backgrounds in developing and distributing blockchain ledger technologies to maintain Tokens. We have not identified all the persons that we will need to engage to provide services and functions critical to maintain the Tokens. We cannot assure that we will be able to engage all such persons with the necessary expertise on the terms acceptable to us, or at all. Further, there can be no assurance

given that if we are able to engage such service providers that they will be able to provide the services and functions meeting our specifications and requirements. If we fail to identify and engage all such service providers or personnel, or if the providers fail to satisfy our specifications and requirements, it could have a material adverse effect on our ability to develop and maintain the Tokens and related technology successfully.

There is currently no trading market for the Tokens, and a trading market may never develop.

There is currently no trading market available for the Tokens and no suitable platform pursuant to which Tokenholders may transfer or resell their Tokens (such a marketplace, a “Designated Marketplace”). Peer-to-peer trading will not be permitted unless and until Tokenholders are notified otherwise by us and informed of the requirements to do so. We are aware of certain Alternative Trading Systems (“ATSs”) that intend to facilitate secondary trading of security tokens, such as tZero and Templum, but we cannot provide any assurances as to whether any such ATS will become and remain operational and facilitate trading of the Tokens. Even if an ATS becomes and remains operational, there is no guarantee that there will be a sufficient number of Tokens outstanding to facilitate a liquid market. As a result, Tokenholders should be prepared to hold their Tokens indefinitely. In the event that the Tokens remain un-tradable indefinitely, the value of the Tokens could be materially adversely affected.

We do not expect there to be any market makers to develop a trading market in the Tokens in the near future.

Most securities that are publicly traded in the U.S. have one or more broker-dealers acting as “market makers” for the security. A market maker is a firm that stands ready to buy and sell the security on a regular and continuous basis at publicly quoted prices. In the event that a Designated Marketplace is created or developed, we do not believe that the Tokens will have any market makers at that time, which could contribute to a lack of liquidity in the Tokens, and could have a material adverse effect on holders’ ability to trade the Tokens. We cannot provide any assurances as to if or when we will be able to appoint any market makers for the Tokens that are satisfactory to us.

The prices of digital assets have been extremely volatile and the Tokens may be subject to significant price volatility.

The prices of digital assets have historically been subject to dramatic fluctuations and are highly volatile, and the market price of the Tokens may also be highly volatile. Several factors may influence the market price, if any, of the Tokens, including, but not limited to:

- the ability of the Tokens to trade in a secondary market, if at all;
- the availability of a Designated Marketplace or other trading platform for digital assets;
- global digital asset and security token supply;
- global digital asset demand, the security of online digital asset exchanges and digital wallets that hold digital assets, the perception that the use and holding of digital assets is safe and secure and the regulatory restrictions on their use;
- changes in the software, software requirements or hardware requirements underlying the Tokens;
- changes in the rights, obligations, incentives or rewards for the various Tokenholders;
- interruptions in service from or failures of major digital asset and security token exchanges on which digital assets and security tokens are traded;
- investment and trading activities of large purchasers, including private and registered funds, that may directly or indirectly invest in securities tokens or other digital assets;
- regulatory measures, if any, that affect the use of digital assets and security tokens such as the Tokens; and
- expectations among digital assets participants that the value of security tokens or other digital assets will soon change.

A decrease in the price of a single digital asset may cause volatility in the entire digital asset and security token industry and may affect other digital assets including the Tokens. Such volatility in the price of the Tokens may result in significant loss over a short period of time.

Tokenholders will generally not have voting rights and will generally have no ability to influence our decisions.

Tokenholders will have no voting rights except as required by Delaware law. As a result, except with respect to matters required to be submitted to Tokenholders under Delaware law, all matters submitted to stockholders will be decided by the vote of holders of our capital stock entitled to vote thereon, which shall not include the Tokens. As a result, Tokenholders will have no ability to elect directors or, except with respect to matters required to be submitted to Tokenholders under Delaware law, to determine the outcome of any other matters submitted to a vote of our stockholders.

We do not expect to pay any dividends on the Tokens.

Dividends will not be paid with respect to the Tokens.

Issuances by us of additional securities, whether in traditional or token format, could affect ownership and voting rights over us. In addition, the issuance of preferred shares, or options or warrants to purchase those preferred shares, could negatively impact the value of the Tokens as the result of preferential dividend rights, conversion rights, redemption rights and liquidation provisions granted to the stockholders of such preferred shares.

From time to time, we may issue in public or private sales additional securities to third party investors. Such securities may provide holders with ownership and voting rights that could provide the holders thereof with substantial influence over the Company and its operations. Any preferred shares that may be issued shall have such rights, preferences, privileges and restrictions as may be designated from time-to-time by our board, including preferential dividend rights, voting rights, conversion rights, redemption rights and liquidation provisions. There cannot be any assurance that we will not issue preferred securities with rights and preferences that are more beneficial than those provided to Tokenholders.

The Tokens will be subject to complex and evolving U.S. and foreign laws and regulations regarding privacy, technology, data protection and other matters. Many of these laws and regulations are subject to change and uncertain interpretation, and could result in claims, increased cost of operations or otherwise harm our business.

The Tokens will be subject to a variety of laws and regulations in the U.S. and abroad, including user privacy, blockchain technology, broker dealer, data protection and intellectual property, among others. Foreign data protection, privacy, broker dealer and other laws and regulations are often more restrictive than those in the U.S. These U.S. federal and state and foreign laws and regulations are constantly evolving and can be subject to significant change. In addition, the application and interpretation of these laws and regulations are often uncertain.

The risk of our being found in violation of these or other laws and regulations in connection with the Tokens is further increased by the fact that many of them have not been fully interpreted by the regulatory authorities or the courts and are open to a variety of interpretations. Any action brought against us for violation of these or other laws or regulations, even if we successfully defend against it, could cause us to incur significant legal expenses and divert our management's attention from the operation of our business. If our operations are found to be in violation of any of these laws and regulations, we may be subject to any applicable penalty associated with the violation, including civil and criminal penalties, damages and fines, we could be required to refund payments received by us, and we could be required to curtail or cease our operations. Any of the foregoing consequences could seriously harm our business and our financial results. These existing and proposed laws and regulations can be costly to comply with and can result in negative publicity, increase our operating costs, require significant management time and attention, and subject us to claims or other remedies, including fines or demands that we modify or ceases existing practices. In addition, due to the novelty of the Tokens and the uncertain and evolving laws and regulations that apply, insurance underwriters may be unwilling to provide coverage for claims relating to the Tokens on terms acceptable to us, if at all. Any claims related to the Tokens or the Offering could have a material adverse effect on our current and future business.

The Staff of the SEC's Division of Enforcement and other regulatory agencies are conducting investigations regarding offerings of securities similar to the Tokens.

Recently, the Division of Enforcement of the SEC and other regulatory agencies have undertaken investigations of offerings of securities similar to the Tokens. Should the SEC or other agency choose to investigate the Offering or Token trading more generally, such investigations could result in delay of the Offering, negative publicity for us, and may have a material adverse effect on our current and future business.

#### Item 1B. Unresolved Staff Comments

None.

Item 2. Properties

We lease our manufacturing, research and development, and corporate offices in Lexington, Massachusetts occupying approximately 82,000 square feet. This lease agreement terminates in August 2023 with an option to renew for one additional ten-year period.

During December 2012 we entered into a commercial lease for approximately 5,600 square feet of office space in New York, New York for use as corporate offices that terminates in May 2020.

We also lease research and office facilities in Cambridge, United Kingdom. This lease terminates in November 2025.

In December 2015, we acquired a manufacturing facility with approximately 24,000 square feet in Berkeley, California to be used in the production and manufacture of antibody product candidates. In December 2015, we also entered into a commercial lease in

Berkeley, California for approximately 10,900 square feet to be used for corporate offices which expires in December 2020. We also have a sublease in Berkeley, California for parking that expires in May 2020.

We believe substantially all of our property and equipment is in good condition and that we have sufficient capacity to meet our current operational needs. We do not anticipate experiencing significant difficulty in retaining occupancy of any of our manufacturing or office facilities and will do so through lease renewals prior to expiration or through replacing them with equivalent facilities.

Item 3. Legal Proceedings

We are not party to any material legal proceedings.

Item 4. Mine Safety Disclosures

Not applicable.



## PART II

## Item 5. Market for Registrant’s Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities

Our common stock is currently listed on The Nasdaq Capital Market under the symbol “AGEN.” As of March 4, 2019, there were 389 holders of record and 25,576 beneficial holders of our common stock.

We have never paid cash dividends on our common stock, and we do not anticipate paying any cash dividends in the foreseeable future. We currently intend to retain future earnings, if any, for the future operation and expansion of our business. Any future payment of dividends on our common stock will be at the discretion of our Board of Directors and will depend upon, among other things, our earnings, financial condition, capital requirements, level of indebtedness, and other factors that our Board of Directors deem relevant.

## Stock Performance

The following graph shows the cumulative total stockholder return on our common stock over the period spanning December 31, 2013 to December 31, 2018, as compared with that of the Nasdaq Stock Market (U.S. Companies) Index and the Nasdaq Biotechnology Index, based on an initial investment of \$100 in each on December 31, 2013. Total stockholder return is measured by dividing share price change plus dividends, if any, for each period by the share price at the beginning of the respective period and assumes reinvestment of dividends.

This stock performance graph shall not be deemed “filed” with the SEC or subject to Section 18 of the Exchange Act, nor shall it be deemed incorporated by reference in any of our filings under the Securities Act of 1933, as amended (the “Securities Act”).

## COMPARISON OF CUMULATIVE TOTAL RETURN OF AGENUS INC.,

## NASDAQ STOCK MARKET (U.S. COMPANIES) INDEX

## AND NASDAQ BIOTECHNOLOGY INDEX

	12/31/2013	12/31/2014	12/31/2015	12/31/2016	12/31/2017	12/31/2018
Agenus Inc.	100.00	150.38	171.97	156.06	123.48	90.15
NASDAQ Stock Market (U.S. Companies) Index	100.00	113.40	119.89	128.89	165.29	158.87
NASDAQ Biotechnology Index	100.00	131.57	149.42	117.02	141.66	128.45

## Item 6. Selected Financial Data

We have derived the condensed consolidated balance sheet data set forth below as of December 31, 2018 and 2017, and the condensed consolidated statement of operations data for each of the years in the three-year period ended December 31, 2018, from our audited consolidated financial statements included elsewhere in this Annual Report on Form 10-K.

You should read the selected condensed consolidated financial data in conjunction with “Management’s Discussion and Analysis of Financial Condition and Results of Operations,” our consolidated financial statements, and the notes to our consolidated financial statements included elsewhere in this Annual Report on Form 10-K.

Changes in cash, cash equivalents, and short-term investments, total current assets, total assets, total current liabilities, long-term debt and stockholders’ (deficit) equity in the periods presented below include the effects of the receipt of net proceeds from our debt offerings, equity offerings, royalty monetization transactions, the exercise of stock options, and employee stock purchases that totaled approximately \$291.2 million, \$81.5 million, \$3.4 million, \$220.4 million, and \$57.0 million in the years ended December 31, 2018, 2017, 2016, 2015, and 2014, respectively.

	For the Year Ended December 31,				
	2018	2017	2016	2015	2014
	(in thousands except per share data)				
<b>Condensed Consolidated Statement of Operations Data:</b>					
Revenue	\$36,784	\$42,877	\$22,573	\$24,817	\$6,977
Operating expenses:					
Research and development	(124,600)	(116,125)	(94,971 )	(70,444)	(22,349)
General and administrative	(37,340 )	(33,741 )	(33,126 )	(28,370)	(21,250)
Contingent purchase price consideration fair value adjustment	1,335	3,188	(1,953 )	(6,704 )	(6,699 )
Operating loss	(123,822)	(103,801)	(107,477)	(80,701)	(43,321)
Loss on early extinguishment of debt	(10,767 )	—	—	—	—
Non-operating income (expense)	(2,183 )	1,977	(2,202 )	(5,968 )	2,096
Interest expense, net	(25,273 )	(18,868 )	(17,316 )	(6,599 )	(1,261 )
Loss before taxes	(162,044)	(120,692)	(126,995)	(93,268)	(42,486)
Income tax benefit (1)	—	—	—	5,387	—
Net loss	(162,044)	(120,692)	(126,995)	(87,881)	(42,486)
Dividends on Series A-1 convertible preferred stock	(207 )	(206 )	(204 )	(203 )	(204 )
Less: net loss attributable to non-controlling interest	(2,352 )	—	—	—	—
Net loss attributable to Agenus Inc. common stockholders	\$(159,899)	\$(120,898)	\$(127,199)	\$(88,084)	\$(42,690)
Net loss attributable to Agenus Inc. common stockholders per common share, basic and diluted	\$(1.44 )	\$(1.23 )	\$(1.46 )	\$(1.13 )	\$(0.71 )
Weighted average number of Agenus Inc. common shares outstanding,					
basic and diluted	110,772	98,415	87,070	78,212	59,754

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	As of December 31,				
	2018	2017	2016	2015	2014
	(in thousands)				
<b>Condensed Consolidated Balance Sheet Data:</b>					
Cash, cash equivalents and short-term investments	\$53,054	\$60,187	\$76,437	\$171,668	\$40,224
Total current assets	74,808	73,554	91,312	184,095	42,670
Total assets	136,401	138,402	156,986	242,228	74,527
Total current liabilities	68,062	56,438	40,851	28,934	9,229
Long-term debt, less current portion	13,212	142,385	130,542	114,326	4,769
Series C-1 convertible preferred stock	39,879	—	—	—	—
Total stockholders' (deficit) equity	(174,546)	(75,816)	(39,126)	70,728	23,018

(1) Given our history of incurring operating losses, no income tax benefit has been recognized in our consolidated statements of operations for the years ended December 31, 2018, 2017, 2016, and 2014 because of the loss before income taxes, and the need to recognize a valuation allowance on the portion of our deferred tax assets which will not be offset by the reversal of deferred

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tax liabilities. For the year ended December 31, 2015, we recognized an income tax benefit as a result of the deferred tax liabilities recognized in connection with the PhosImmune and XOMA antibody manufacturing facility acquisitions.

Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations  
Overview

Agenus Inc. (including its subsidiaries, collectively referred to as "Agenus," the "Company," "we," "us," and "our") is a clinical-stage immuno-oncology ("I-O") company with a pipeline of immune modulating antibodies, cancer vaccines, adjuvants and adoptive cell therapies dedicated to becoming a leader in the discovery and development of innovative combination therapies and committed to bringing effective medicines to patients with cancer. Our business is designed to drive success in I-O through speed, innovation, and effective combination therapies. In addition to a diverse pipeline we have assembled fully integrated capabilities including novel target discovery, antibody generation, cell line development, and good manufacturing practice ("GMP") manufacturing. We believe that these fully integrated capabilities enable us to produce novel candidates on timelines that are shorter than the industry standard. Leveraging from our science and capabilities we have forged important partnerships to advance our innovation.

We are developing a comprehensive I-O portfolio driven by the following platforms and programs, which we intend to utilize individually and in combination:

- our antibody discovery platforms, including our Retrocyte Display™, SECAN<sup>®</sup> yeast display, and phage display technologies designed to drive the discovery of future CPM antibody candidates;
- our antibody candidate programs, including our CPM programs;
- our vaccine programs, including Prophage™, AutoSynVax™ and PhosphoSynVax™;
- our saponin-based vaccine adjuvants, principally our QS-21 Stimulon<sup>®</sup> adjuvant, or QS-21 Stimulon; and
- our cell therapy subsidiary, AgenTus Therapeutics, which is designed to drive the discovery of future adoptive cell therapy, or "living drugs" (CAR-T and TCR) programs.

We assess development, commercialization and partnering strategies for each of our product candidates periodically based on several factors, including pre-clinical and clinical trial results, competitive positioning and funding requirements and resources. We are currently advancing our proprietary anti-CTLA-4 and anti-PD-1 antibodies in trials that are designed to be registrational and to support one or more BLA filings as soon as 2020.

We have formed collaborations with companies such as Incyte Corporation ("Incyte"), Merck Sharpe & Dohme ("Merck") and Recepta Biopharma SA ("Recepta"). Through these alliances, as well as our own internal programs, we currently have more than a dozen antibody programs in pre-clinical or clinical development, including our anti-CTLA-4 and anti-PD-1 antibody programs (both partnered with Recepta for certain South America territories) and anti-GITR and anti-OX40 antibody programs (both partnered with Incyte). In February 2017, we amended our collaboration agreement with Incyte to, among other things, convert the GITR and OX40 programs from profit-share to royalty-bearing programs, and there are no longer any profit-share programs remaining under the collaboration. Pursuant to the amended agreement, we received accelerated milestone payments of \$20.0 million from Incyte related to the clinical development of INCAGN1876 (anti-GITR agonist) and INCAGN1949 (anti-OX40 agonist). Concurrent with the execution of the amendment, we and Incyte also entered into the Stock Purchase Agreement whereby Incyte purchased an additional 10 million shares of our common stock at \$6.00 per share, resulting in additional proceeds of \$60.0 million to us. On September 20, 2018, we, through our wholly-owned subsidiary, Agenus Royalty Fund, LLC, entered into a Royalty Purchase Agreement (the "XOMA Royalty Purchase Agreement") with XOMA (US) LLC ("XOMA"). Pursuant to the terms of the XOMA Royalty Purchase Agreement, XOMA paid us \$15.0 million at closing in exchange for the right to receive 33% of the future royalties and 10% of the future milestones that we are entitled to receive from Incyte and Merck, net of certain of our obligations to a third party and excluding the next milestone that we expect to receive from Incyte. After taking into account our obligations under the XOMA Royalty Purchase Agreement, as of December 31, 2018, we remain eligible to receive up to \$450.0 million and \$85.5 million in potential development, regulatory and commercial milestones from Incyte and Merck, respectively.

In December 2018, we entered into a series of agreements with Gilead Sciences, Inc. ("Gilead") to collaborate on the development and commercialization of up to five novel I-O therapies. Pursuant to the collaboration agreements, we received an upfront cash payment from Gilead of \$120.0 million following the closing in January 2019 and are

eligible to receive up to an additional \$1.7 billion in aggregate potential fees and milestones. At closing, Gilead received worldwide exclusive rights to our bispecific antibody, AGEN1423. Gilead also received the exclusive option to license exclusively AGEN1223, a bispecific antibody, and AGEN2373, a monospecific antibody. We recently filed INDs for AGEN1423 and AGEN1223 and are planning to file an IND for AGEN2373 in the first half of 2019. We are responsible for developing the option programs up to the option decision points, at which time Gilead may acquire exclusive rights to the programs on option exercise. For either, but not both, of the option programs, we have the right to opt-in to share Gilead's development and commercialization costs in the United States in exchange for a profit (loss) share on a 50:50 basis and revised milestone payments. Gilead also received the right of first negotiation for two additional,

undisclosed preclinical programs. At the closing, Gilead also purchased 11,111,111 shares of Agenus common stock for \$30.0 million pursuant to a stock purchase agreement.

In addition to our antibody platforms and CPM programs, we are also advancing a series of vaccine programs to treat cancer. In January 2017, we announced a clinical trial collaboration with the National Cancer Institute (“NCI”), which is a double-blind, randomized controlled Phase 2 trial that is evaluating the effect of our autologous vaccine candidate, Prophage, in combination with pembrolizumab (Keytruda®, Merck & Co., Inc. (“Merck”)) in patients with newly diagnosed glioblastoma. Under this collaboration, we are supplying Prophage, Merck is supplying pembrolizumab and the NCI and Brain Tumor Trials Collaborative member sites are recruiting patients and conducting the trial.

Our QS-21 Stimulon adjuvant is partnered with GlaxoSmithKline (“GSK”) and is a key component in multiple GSK vaccine programs. These programs are in various stages, with the most advanced being GSK’s shingles vaccine, Shingrix. In 2015, we monetized a portion of the future royalties we were contractually entitled to receive from GSK from sales of its shingles and malaria vaccines through a Note Purchase Agreement (“NPA”) and received net proceeds of approximately \$78 million. In October 2017, GSK’s shingles vaccine was approved in the United States by the FDA and granted marketing authorization in Canada by Health Canada, and in November 2017, we exercised our option to issue the \$15.0 million in additional notes in accordance with the terms of the NPA. In January 2018, we entered into a Royalty Purchase Agreement with Healthcare Royalty Partners III, L.P. and certain of its affiliates (together, “HCR”), pursuant to which HCR purchased 100% of our worldwide rights to receive royalties from GSK on GSK’s sales of vaccines containing our QS-21 Stimulon adjuvant. We used the majority of the upfront proceeds from HCR to redeem all of the notes issued pursuant to the NPA, resulting in net proceeds to us of approximately \$28.0 million at closing. We do not incur clinical development costs for products partnered with GSK. Pursuant to our agreement with HCR, we are entitled to receive up to \$40.35 million in milestone payments based on GSK’s sales of Shingrix as follows: (i) \$15.1 million upon reaching \$2.0 billion last-twelve-months net sales any time prior to 2024 and (ii) \$25.25 million upon reaching \$2.75 billion last-twelve-months net sales any time prior to 2026. We are also obligated to pay HCR approximately \$25.9 million in 2021 if neither of the following Shingrix sales milestones are achieved: (i) 2019 sales exceed \$1.0 billion or (ii) 2020 sales exceed \$1.75 billion. GSK began selling Shingrix commercially in the fourth quarter of 2017. In February 2019, GSK reported that Shingrix sales for 2018, its first full year on the market, were over \$1.0 billion.

Our business activities include product research and development, intellectual property prosecution, manufacturing, regulatory and clinical affairs, corporate finance and development activities, and support of our collaborations. Our product candidates require clinical trials and approvals from regulatory agencies, as well as acceptance in the marketplace. Part of our strategy is to develop and commercialize some of our product candidates by continuing our existing arrangements with academic and corporate collaborators and licensees and by entering into new collaborations.

In October 2017, we announced the launch of a subsidiary that is advancing our cell therapy business, AgenTus Therapeutics. The subsidiary is focused on the discovery, development, and commercialization of breakthrough “living drugs” to advance cures for cancer patients. AgenTus Therapeutics licenses intellectual property assets from Agenus and has its own management and governance.

Our common stock is currently listed on The Nasdaq Capital Market under the symbol “AGEN.”

Our research and development expenses for the years ended December 31, 2018, 2017, and 2016, were \$124.6 million, \$116.1 million, and \$95.0 million, respectively. We have incurred significant losses since our inception. As of December 31, 2018, we had an accumulated deficit of \$1.18 billion.

To date, we have financed our operations primarily through the sale of equity and debt securities. We believe that, based on our current plans and activities, including additional funding we received in connection with our transactions with Gilead subsequent to December 31, 2018, our cash on-hand will be sufficient to satisfy our liquidity requirements

for more than one year from when these financial statements were issued. We may attempt to raise additional funds by: (1) pursuing collaboration, out-licensing and/or partnering opportunities for our portfolio programs and product candidates with one or more third parties, (2) renegotiating third party agreements, (3) selling assets, (4) securing additional debt financing and/or (5) selling equity securities. Satisfying long-term liquidity needs may require the successful commercialization and/or substantial out-licensing or partnering arrangements for our antibody discovery platforms, CPM antibody programs, and HSP-based vaccines. Our long-term success will also be dependent on the successful identification, development and commercialization of potential other product candidates, each of which will require additional capital with no certainty of timing or probability of success. If we incur operating losses for longer than we expect, and/or we are unable to raise additional capital, we may become insolvent and be unable to continue our operations.

#### Historical Results of Operations

Year Ended December 31, 2018 Compared to the Year Ended December 31, 2017

Research and development revenue

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We recognized research and development (“R&D”) revenue of approximately \$19.5 million and \$42.7 million during the years ended December 31, 2018 and 2017, respectively. R&D revenues for the year ended December 31, 2018, primarily consisted of fees earned under our Collaboration Agreement with Incyte, including \$10.0 million related to the recognition of milestones and \$4.1 million related to the reimbursement of development costs, which have decreased due to the stage of the programs under the collaboration, and \$4.0 million related to the recognition of a milestone under our license agreement with Merck. R&D revenues for the year ended December 31, 2017, also primarily consisted of fees earned under our Collaboration Agreement with Incyte including \$20.0 million related to the acceleration of milestone payments and \$14.6 million related to the reimbursement of development costs in addition to \$4.0 million related to the recognition of a milestone under our license agreement with Merck, \$1.0 million related to the recognition of a milestone under our license agreement with GSK. During the years ended December 31, 2018 and 2017, we recorded revenue of \$1.3 million and \$3.1 million, respectively, from the amortization of deferred revenue. See Notes 2 and 14 to our Consolidated Financial Statements for additional discussion of our revenues, including the adoption of ASC 606 during the first quarter of 2018.

#### Non-cash royalty revenue related to the sale of future royalties

In January 2018, we sold 100% of our worldwide rights to receive royalties from GSK on sales of GSK’s vaccines containing our QS-21 Stimulon adjuvant to HCR. As described in Note 18 to our Consolidated Financial Statements, this transaction has been recorded as a liability that amortizes over the estimated life of our Royalty Purchase Agreement with HCR. As a result of this liability accounting, even though the royalties are remitted directly to HCR, we record these royalties from GSK as revenue. During the year ended December 31, 2018, we recognized approximately \$17.3 million in non-cash royalty revenue related to our agreement with GSK.

#### Research and development expense

Research and development expense include the costs associated with our internal research and development activities, including compensation and benefits, occupancy costs, clinical manufacturing costs, contract research organization costs, costs of consultants, and related administrative costs. Research and development expense increased 7% to \$124.6 million for the year ended December 31, 2018 from \$116.1 million for the year ended December 31, 2017. Increased expenses in the year ended December 31, 2018 primarily relate to a \$7.3 million increase in third-party services and other related expenses largely relating to the advancement of our antibody programs and a \$3.0 million increase in expenses attributable to the activities of our subsidiaries, AgenTus Therapeutics and our wholly-owned subsidiary in the United Kingdom, Agenus UK Limited, which increase was partially offset by a decrease in expenses due to the closure of our facility in Basel, Switzerland in 2017. These increases were partially offset by a \$1.6 million decrease in personnel related expenses, which consists of a \$2.8 million decrease in share based compensation expense partially offset by a \$1.2 million increase in other personnel related expenses, and a \$0.3 million decrease in other R&D expenses.

#### General and administrative expense

General and administrative expense consists primarily of personnel costs, facility expenses, and professional fees. General and administrative expense increased 11% to \$37.3 million for the year ended December 31, 2018 from \$33.7 million for the year ended December 31, 2017. Increased general and administrative expense in 2018 primarily relates to a \$1.9 million increase in professional fees, a \$1.0 million increase in other G&A expenses, and a \$1.0 million increase in expenses attributable to the activities of our subsidiaries, AgenTus Therapeutics and our wholly-owned subsidiary in the United Kingdom, Agenus UK Limited, which increase was partially offset by a decrease in expenses due to the closure of our facility in Basel, Switzerland in 2017. These increases were partially offset by a \$0.3 million decrease in personnel related expenses, which consists of a \$1.9 million decrease in share based compensation expense partially offset by a \$1.7 million increase in other personnel related expenses.

#### Contingent purchase price consideration fair value adjustment

Contingent purchase price consideration fair value adjustment represents the change in the fair value of our contingent purchase price consideration during the year ended December 31, 2018, which resulted from changes in our market capitalization and share price and changes in the credit spread since the prior year end. The fair value of our contingent purchase price consideration is based on estimates from a Monte Carlo simulation of our market capitalization and share price.

Loss on early extinguishment of debt

Loss on early extinguishment of debt of \$10.8 million for the year ended December 31, 2018 represents the payment of premiums and the write-off of unamortized debt issuance costs and discounts incurred in connection with the full redemption and termination of Antigenics' \$115.0 million principal amount of notes issued pursuant to the Note Purchase Agreement dated September 4, 2015 with Oberland Capital SA Zermatt LLC and the purchasers named therein.

#### Non-operating income (expense)

Non-operating expense increased \$4.2 million for the year ended December 31, 2018, from income of \$2.0 million for the year ended December 31, 2017, to expense of \$2.2 million for the year ended December 31, 2018, primarily due to our increased foreign currency exchange losses in 2018 compared to gains in 2017.

#### Interest expense, net

Interest expense, net increased to \$25.3 million for the year ended December 31, 2018 from \$18.9 million for the year ended December 31, 2017 due to the January 2018 closing of the Royalty Purchase Agreement with HCR and the resulting increase in non-cash interest expense compared to the amount recorded for our Note Purchase Agreement, which was outstanding in the year ended December 31, 2017, and fully redeemed and terminated simultaneously with the closing of the Royalty Purchase Agreement.

#### Year Ended December 31, 2017 Compared to the Year Ended December 31, 2016

##### Research and development revenue

We recognized research and development revenue of approximately \$42.7 million and \$22.4 million during the years ended December 31, 2017 and 2016, respectively. R&D revenues primarily included fees earned under our license agreements, including approximately \$14.6 million and \$16.2 million for the years ended December 31, 2017, and 2016, respectively, related to reimbursement of development costs under our Collaboration Agreement with Incyte. The increase in total revenue for the year ended December 31, 2017 is primarily attributable to the \$20.0 million in accelerated milestones, recognized as revenue during the twelve months ended December 31, 2017, related to the antibody candidates targeting GITR and OX40 received in connection with the February 14, 2017 amendment to our License, Development and Commercialization Agreement with Incyte. During the years ended December 31, 2017 and 2016, we recorded revenue of \$3.1 million and \$3.5 million, respectively, from the amortization of deferred revenue.

##### Research and development expense

Research and development expense increased 22% to \$116.1 million for the year ended December 31, 2017 from \$95.0 million for the year ended December 31, 2016. Increased expenses in 2017 primarily relate to a \$17.6 million increase in third-party services and other expenses relating largely to the advancement of our CPM antibody programs, a \$3.3 million increase in payroll related costs primarily due to increased headcount, and a \$0.6 million increase in depreciation expense, offset by a \$0.4 million decrease in expense for our foreign subsidiaries due to the closure of our facility in Basel, Switzerland, which decrease was partially offset by increased expenses attributable to Agenus UK.

##### General and administrative expense

General and administrative expenses increased 2% to \$33.7 million for the year ended December 31, 2017 from \$33.1 million for the year ended December 31, 2016. Increased general and administrative expenses in 2017 primarily relate to a \$1.8 million increase in payroll related costs primarily due to increased headcount offset by a \$0.6 million decrease in professional fees due to the reduced use of consultants and a \$0.6 million decrease in expense for our foreign subsidiaries due to the closure of our facility in Basel, Switzerland, which decrease was partially offset by increased expenses attributable to Agenus UK.

##### Contingent purchase price consideration fair value adjustment

Contingent purchase price consideration fair value adjustment represents the change in the fair value of our contingent purchase price consideration during the year ended December 31, 2017, which resulted from changes in our market capitalization and share price and changes in the credit spread since the prior year end. The fair value of our contingent purchase price consideration is based on estimates from a Monte Carlo simulation of our market capitalization and share price.

Non-operating income (expense)

Non-operating income increased by \$4.2 million for the year ended December 31, 2017, from an expense of \$2.2 million for the year ended December 31, 2016, to income of \$2.0 million for the year ended December 31, 2017, primarily due to our increased foreign currency exchange gains in 2017 compared to losses in 2016.

Interest expense, net

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Interest expense net increased to \$18.9 million for the year ended December 31, 2017 from \$17.3 million for the year ended December 31, 2016 due to the compounding of interest on our debt under our Note Purchase Agreement and the issuance of additional notes under our NPA in November 2017.

#### Inflation

We believe that inflation has not had a material adverse effect on our business, results of operations, or financial condition to date.

#### Research and Development Programs

For the year ended December 31, 2018, our research and development programs consisted largely of our CPM antibody programs as indicated in the following table (in thousands).

Research and Development Program	Product	For the Year Ended December 31,			Prior to	
		2018	2017	2016	2016	Total
Heat shock proteins for cancer	Prophage					
	and ASV	\$13,235	\$12,499	\$8,202	\$315,189	\$349,125
Antibody programs*	Various	97,011	95,656	83,920	76,712	353,299
Vaccine adjuvant	QS-21					
	Stimulon	211	222	77	13,799	14,309
Other research and development programs		14,143	7,748	2,772	67,822	92,485
<b>Total research and development expenses</b>		<b>\$124,600</b>	<b>\$116,125</b>	<b>\$94,971</b>	<b>\$473,522</b>	<b>809,218</b>

\*Prior to 2014, costs were incurred by 4-AB, which we acquired in February 2014.

Research and development program costs include compensation and other direct costs plus an allocation of indirect costs, based on certain assumptions and our review of the status of each program. Our product candidates are in various stages of development and significant additional expenditures will be required if we start new clinical trials, encounter delays in our programs, apply for regulatory approvals, continue development of our technologies, expand our operations, and/or bring our product candidates to market. The total cost of any particular clinical trial is dependent on a number of factors such as trial design, length of the trial, number of clinical sites, number of patients, and trial sponsorship. The process of obtaining and maintaining regulatory approvals for new therapeutic products is lengthy, expensive, and uncertain. Because our CPM antibody programs are early stage, and because further development of HSP-based vaccines is dependent on clinical trial results, among other factors, we are unable to reliably estimate the cost of completing our research and development programs or the timing for bringing such programs to various markets or substantial partnering or out-licensing arrangements, and, therefore, when, if ever, material cash inflows are likely to commence. Active programs involving QS-21 Stimulon depend on our licensee successfully completing clinical trials, successfully manufacturing QS-21 Stimulon to meet demand, obtaining regulatory approvals and successfully commercializing product candidates containing QS-21 Stimulon.

## Product Development Portfolio

### Antibody Discovery Platforms and CPM Programs

Checkpoint antibodies regulate immune response against pathogens that invade the body and are achieving positive outcomes in a number of cancers that were untreatable only a few years ago. Two classes of checkpoint targets include:

1. inhibitory checkpoints that help suppress an immune response in order to prevent excessive immune reaction resulting in undesired inflammation and/or auto-immunity, and
2. stimulatory checkpoints that can enhance or amplify an antigen-specific immune response.

We possess a suite of antibody discovery platforms that are designed to drive the discovery of future CPM antibody candidates. We are planning to employ a variety of techniques to identify and optimize mono-specific and multi-specific antibody candidates, internally.

We and our partners currently have more than a dozen antibody programs in pre-clinical or clinical development, including our anti-CTLA-4 and anti-PD-1 antibody programs (both partnered with Recepta for certain South America territories) and anti-GITR, anti-OX40, anti-LAG3 and anti-TIM3 antibody programs (all partnered with Incyte). For additional information regarding our

antibody discovery platforms and checkpoint antibody program, please read Part I-Item 1. “Business” of this Annual Report on Form 10-K.

### Prophage Vaccine Candidates

Our early vaccine technology, Prophage (HSPPC-96), is an autologous cancer vaccine therapy derived from cancer tissues that are surgically removed from an individual patient designed to contain a broad sampling of potentially antigenic mutant proteins to educate the patient’s immune system to seek out and destroy cancer. To date, more than 1,000 patients have been treated with Prophage. Data reported at ASCO in 2015 demonstrated that patients with newly diagnosed GBM (ndGBM) with lower immune suppression (measured by peripheral PD-L1 expression) had an improved response to vaccine. To further explore these findings, we announced a Phase 2 clinical trial collaboration with the National Cancer Institute (“NCI”) to evaluate Prophage in combination with pembrolizumab (Keytruda®). The trial is being conducted by the Brain Tumor Trials Collaborative (“BTTC”), led by Dr. Mark Gilbert, Chief of the Neuro-Oncology Branch at the NCI Center for Cancer Research with product provided by Agenus and Merck. The trial is ongoing. For additional information regarding regulatory risks and uncertainties, please read the risks identified under Part I-Item 1A. “Risk Factors” of this Annual Report on Form 10-K.

### Neoantigen Vaccine Platforms

Our neoantigen vaccine platforms include: (i) individualized AutoSynVax™ (ASV™), which targets the unique antigens expressed by a patient’s own tumor, and (ii) off-the-shelf (or pre-manufactured) PhosphoSynVax™ (PSV™), which targets antigens expressed across patients and tumors, potentially enabling us to treat broader categories of patients.

Mutation-based neo-epitopes, which will form the basis for the immunogens used in ASV, appear to be almost always particular to a given patient. Therefore, ASV is a largely individualized vaccine product candidate. With a small amount of a patient’s tumor as a sample, our ASV program is designed to utilize next generation sequencing technologies coupled with complex bioinformatics algorithms to identify mutations in a tumor’s DNA and RNA. Once these mutations have been identified, we plan to manufacture synthetic peptides encoding these neoepitopes, load these peptides on to our recombinant HSP70 and deliver a fully synthetic polyvalent vaccine to the patient. This program is based on the hypothesis that the HSP70 platform would shuttle the mutated peptides to sites where they could be recognized by the immune system and elicit a cytotoxic and helper T cell response in patients with cancer.

Biochemically based neoantigens, such as those arising from dysregulated phosphorylation of various proteins in malignant cells, can serve as a tumor fingerprint across a broad histology of tumors. Through our acquisition of PhosImmune, we have a portfolio of proprietary phosphorylated antigenic targets that can be used for therapeutic development. PSV is a vaccine candidate designed to induce immunity against this novel class of tumor specific neoepitopes known as Phosphopeptides or PTTs. PSV is intended to induce cellular immunity to abnormal Phosphopeptide neoepitopes that are characteristic of these various forms of cancer. We believe PTTs are among the most promising candidates for anti-cancer immunity, as patients with PTT immunity have been shown to have better outcomes than those without PTT immunity. We have amassed a proprietary library of more than 2,000 PTTs. Many of these PTTs are shared among many cancer patients and across multiple tumor types. We are using these PTTs for developing multiple off-the-shelf vaccines. PSV is based on Agenus’ vaccine platform and includes our proprietary QS-21 Stimulon adjuvant and heat-shock protein backbone. Agenus is developing multiple indication-specific PSV offerings, with lead programs in acute myeloid leukemia (AML) and colorectal cancer (CRC). By leveraging our proprietary vaccine platform which has already demonstrated clinical safety and immunogenicity, we intend to advance at least one PSV formulation into the clinic in 2019. For additional information regarding our Neoantigen Vaccine Platforms, please read Part I-Item 1. “Business” of this Annual Report on Form 10-K.

### QS-21 Stimulon Adjuvant

QS-21 Stimulon is an adjuvant, which is a substance added to a vaccine or other immunotherapy that is intended to enhance an immune response to the target antigens. QS-21 Stimulon is a natural product, a triterpene glycoside, or saponin, purified from the bark of the Chilean soapbark tree, *Quillaja saponaria*. QS-21 Stimulon has the ability to stimulate an antibody-mediated immune response and has also been shown to activate cellular immunity. It has become a key component in the development of investigational preventive va